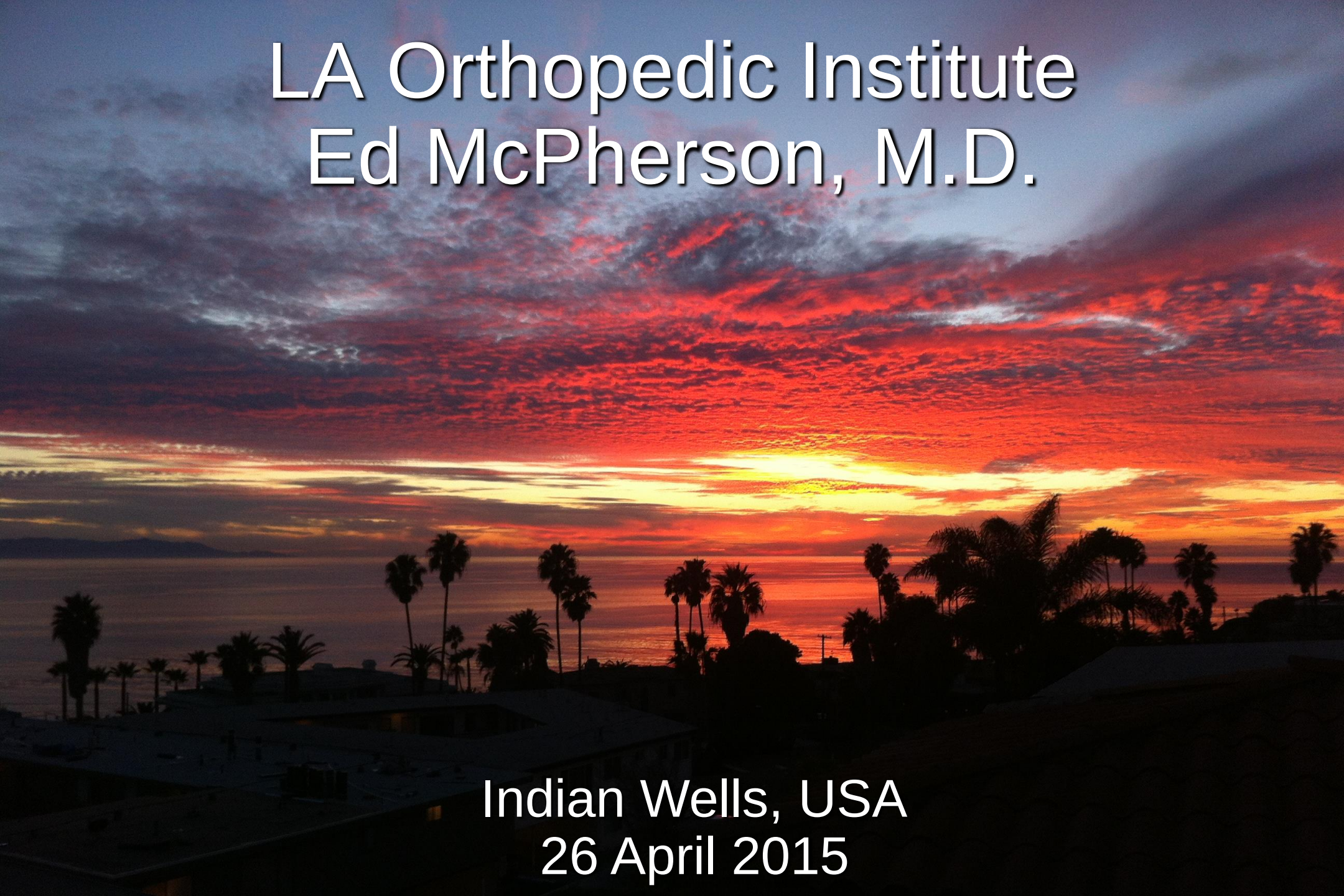

LA Orthopedic Institute
Ed McPherson, M.D.
Indian Wells, USA
26 April 2015

AAOS 2015

Disclosures

- Biocomposites LLC UK
- Biomet Inc.
- Concept Design Development LLC
- Joint Implant Surg Research Found.
- Miller Orthopaedic Review

Thank You HOA Members

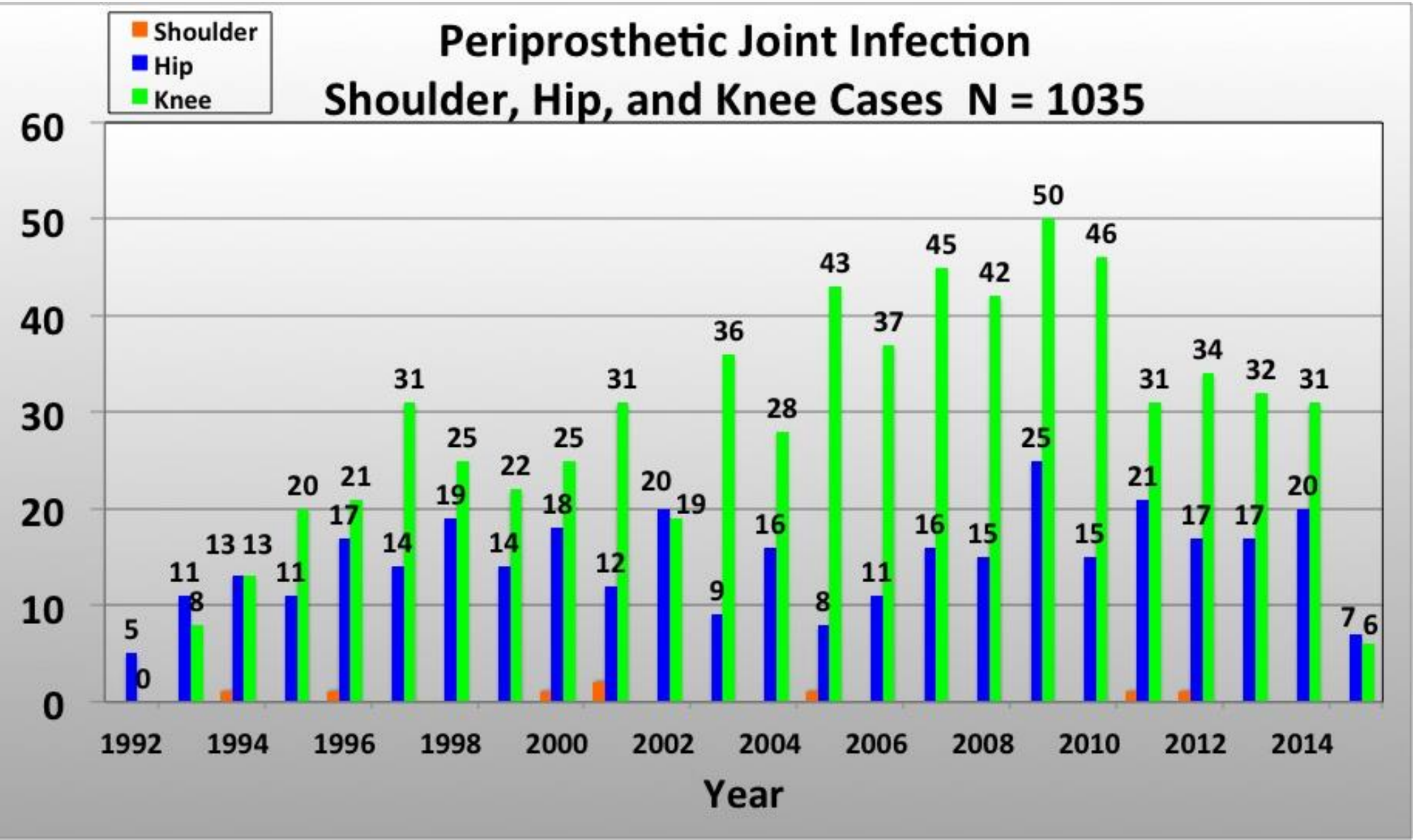
Thank You
Joe Varcadipane
Aipa
Buttons

California Orthopaedic Association

Prosthetic Joint Infection (PJI)

Current Concepts & Trends

Indian Wells, USA
26 April 2015


Shoulder
Hip
Knee
Periprosthetic Joint Infection
Shoulder, Hip, and Knee Cases N = 1035
60
50
40
30
20
10
0
5
0
11
8
13
13
11
20
17
21
14
31
19
25
14
22
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19
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36
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28
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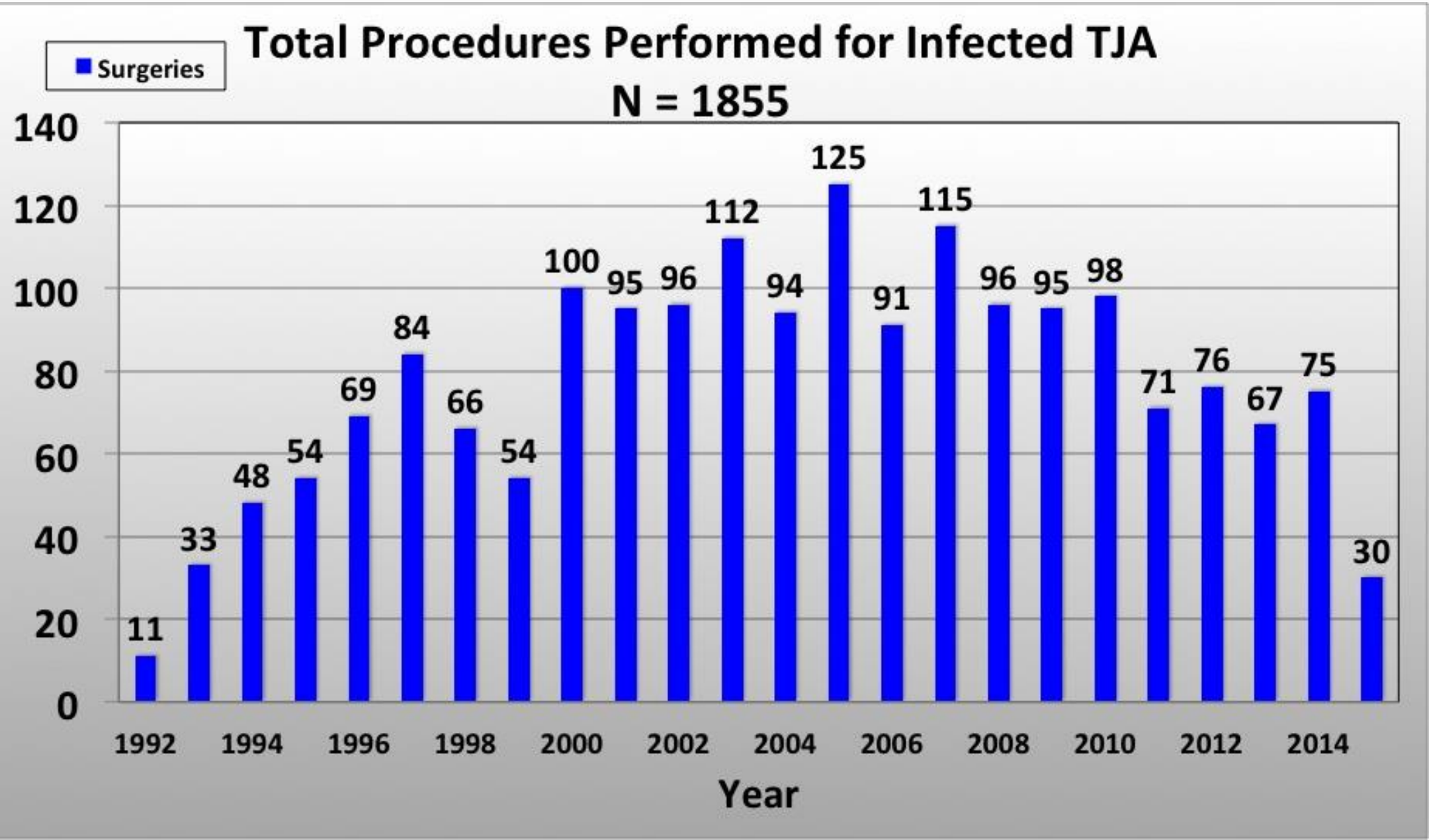
2010
2012
2014
Year


Total Procedures Performed for Infected TJA
N = 1855
Surgeries
140
120
100
80
60
40
20
0
11
33
48
54
69
84
66
54
100
95
96
112
94
125
91
115
96
95
98
71
76
67
75
30
1992
1994
1996
1998
2000
2002
2004
2006
2008
2010
2012
2014
Year

27 Janurary 1941


Rothman Institute at Jefferson Welcomes
Delegates of the
International Consensus Meeting
R
Rothman Institute
at Jefferson

Periprosthetic Joint Infection

Economic Impact

- A two salvage protocol can cost upward of US $250-300K

Ries M. JA 21:308 06’

Ries M. JBJS 87A:1746 05’

Periprosthetic Joint Infection

Why is this important to You!

- We are all now being monitored
- Readmissions & complications
  - infection is going to be given a high priority by cms review
  - physician & facility black balls

Best Tool → Claw Backs

Operating Room

Myths

- You are operating in a sterile environment
- You are operating in a sterile field
  - well, underneath the skin, it started sterile

Mars Curiosity

Sterilization

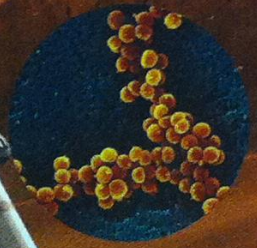
- EtOH scrub
- Bake 230° F
- 56,440 organisms
  - 377 bacterial species

Bateria are Robust

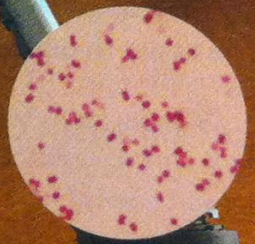
TYPES OF BACTERIA FOUND ON *CURIOSITY*

Gracilibacillus
These organisms may eat perchlorates—salts used in rocket fuel that also occur naturally in Martian soil—for breakfast. Enough said.

Pseudomonas
Humans can go a few days without water; these bacteria can last weeks. Some species have been found to be resistant to antibiotics such as penicillin.



Staphylococcus
Beyond occupying open wounds, colonies of staph can thrive in water more than six times saltier than Earth's oceans.



Moraxella
These bacteria often infect sinuses and lungs. Half the *Curiosity* sample emerged intact from an hour-long bath in hydrogen peroxide.

Streptomyces
Strep colonies (not the ones that cause strep throat) can grow in media spiked with sodium hydroxide, e.g., lye, which is

What Have I Learned

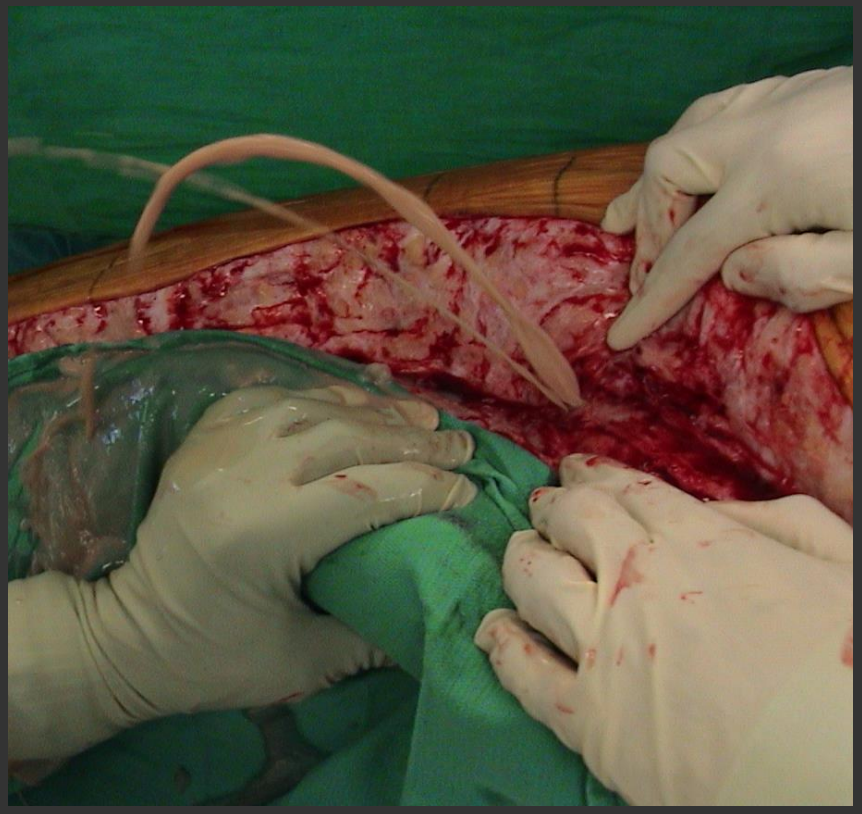
Biofilm

- Biofilm on implants is the cause of chronic disease
- Understanding biofilm enlightens one to logical treatment

What Have I Learned

Host Stratification

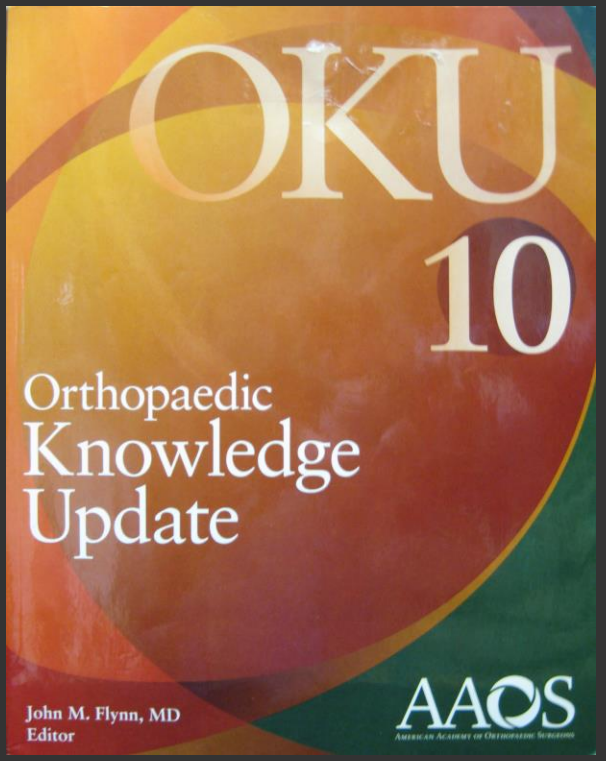
- PJI can be stratified & categorized
  - PJI staging
- Focus on the host, not the bug



Infection Pathomechanics

Host Staging “C Host”

- MSIS-A
  - Staging for PJI
  - Host A-B-C
  - Wound 1-2-3
  - OKU 10



McPherson, EJ. Infection OKU 10 385 11’

What Have I Learned

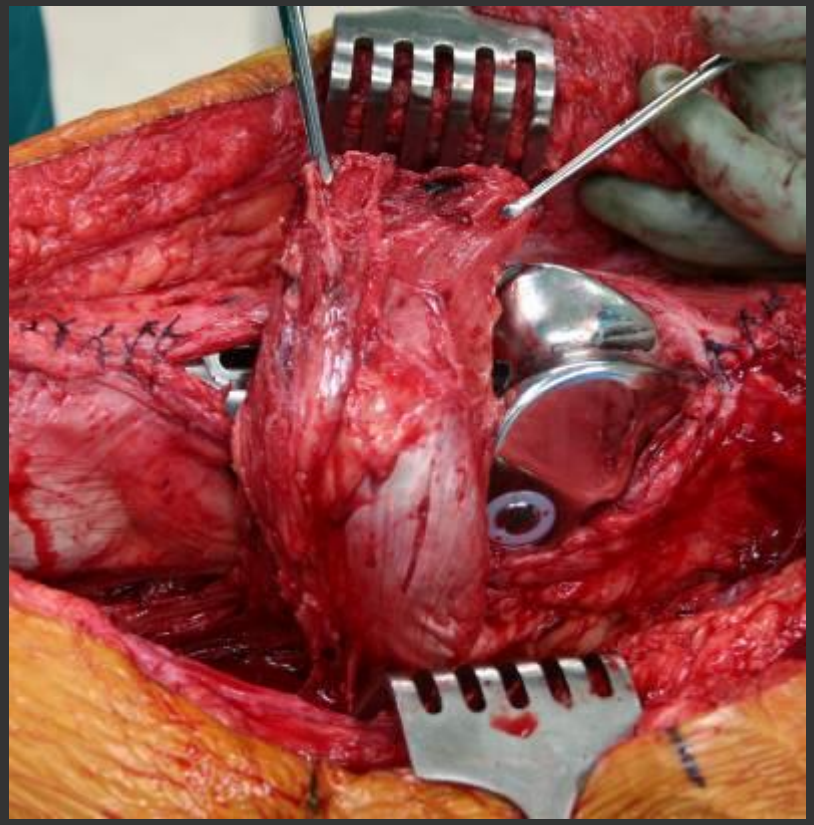
Antibiotic Spacer

- A functional antibiotic loaded cement spacer is a great multipurpose device

What Have I Learned

Muscle Flap

- Soft tissue compromise requires aggressive treatment
- Defects should be filled with muscle flaps

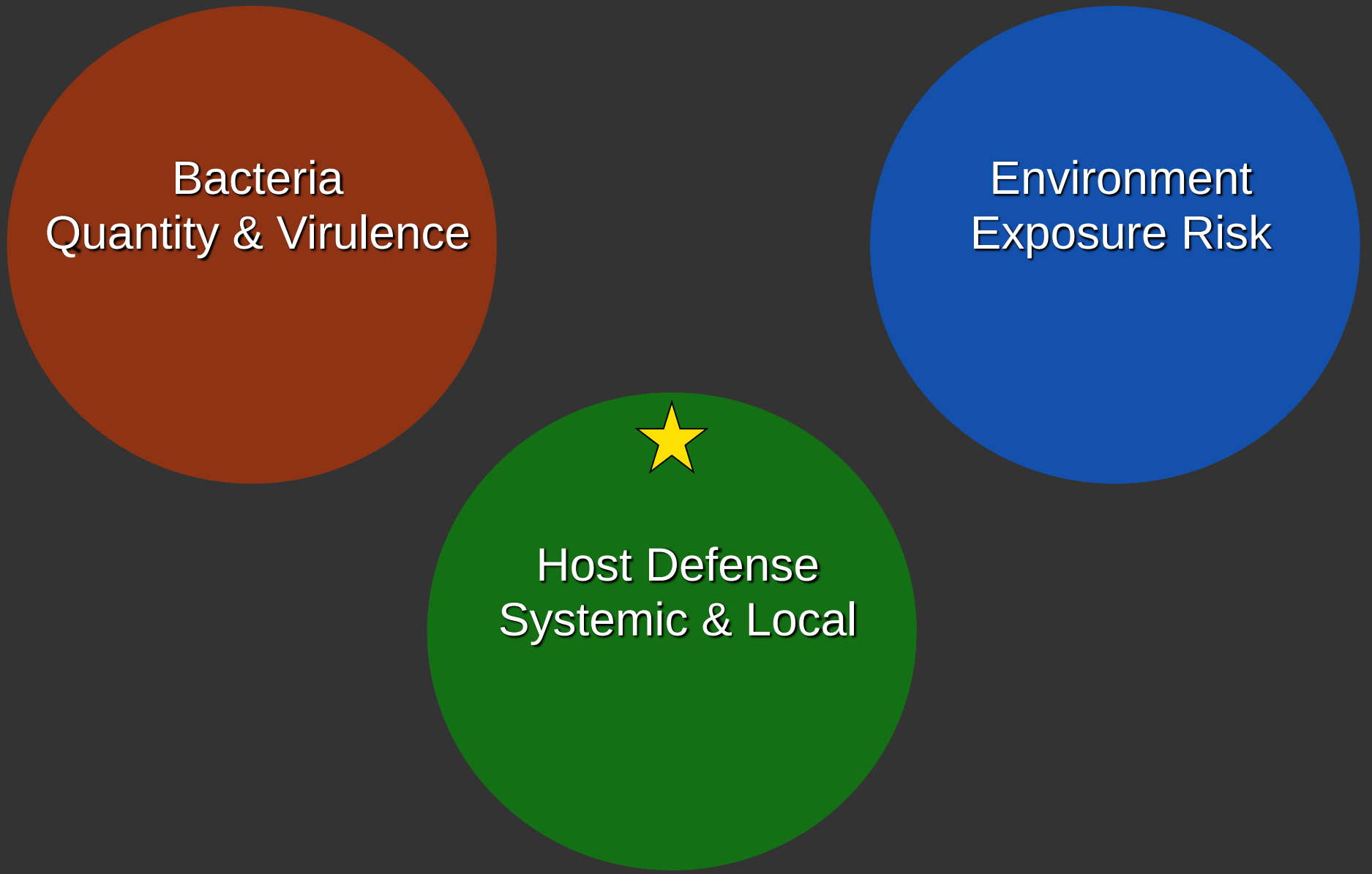


We All Agree

PJI Infection

- Majority of infections occur via bacterial inoculation at the time of surgery
- Some infections occur via bacterial inoculation through open draining wounds

Infection Pathomechanics



Infection Pathomechanics

Operating Room

- Bacteria are shed by operating room personnel
- In an empty room, bacteria settle to floor/walls and stick
  - bacteria don't fly back up like dust

Ritter MA CORR 111:147 75'

Infection Pathomechanics

Bacterial Shedding

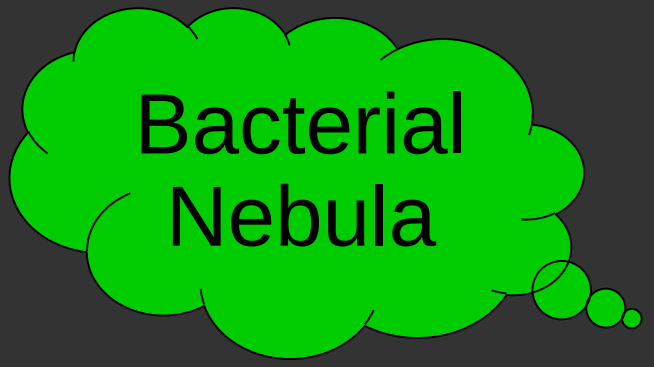
- Shedding rate is genetically determined
  - range 10^3 to 10^4 organisms/minute
  - male > females
  - “shedders” > 10^4 organisms/minute

Bethune DN Lancet 1:480 75’

Infection Pathomechanics

Bacterial Quantity OR

- Bacteria delivery
  - number of personnel
  - shedding rate
- Bacteria elimination
  - filtration
  - UV deactivation



My OR Class 7

Infection Pathomechanics

Bacterial Quantity OR

- OR room with HEPA
  - 299,220 partic/m^3
  - class 7
- OR room horizontal laminar flow
  - 460 partic/m^3
  - class 5

Infection Pathomechanics

Bacterial & Foreign Bodies

- Staph bacteria on a foreign material within the body can enhance an infection by 10,000 fold
  - multiple adhesion mechanisms

Elek S.D. Brit J Exp Path 38:573 57'

Bacteria Management OR

Don’t Assume Everyone Is Conscientious

THE WALL STREET JOURNAL.
WSJ.com

OPINION | JANUARY 8, 2009

Hospital Scrubs Are a Germy, Deadly Mess

Bacteria on doctor uniforms can kill you.

_-~_bqpv~j ``^r debv

You see them everywhere -- nurses, doctors and mec
buses and trains in them, go to restaurants in them,
the bacteria that could kill you.

Dirty scrubs spread bacteria to patients in the hospit
as restaurants. Some hospitals now prohibit wearing
increase in an infection called "C. diff." A national h
difficile (C. diff) infections are sickening nearly half
estimates.

Cover Until Use

Bacteria Management OR

Ancillary Personnel

- Minimize turbulent flow
  - keep doors shut
  - prepare before cut → stay in room
  - relax and sit still
  - beepers & cell phones - off

Traffic Flow 100% Consensus

Bacteria Management OR

Short Exposure Time

- Efficient joint team
- C host → A Game

Efficiency
The Economy of Motion

Bacteria Management OR

Bacterial Inoculation OR

- Local wound lavage with abx saline
- Systemic abx with local blood flow delivery
- Abx delivery via PMMA or $CaSO_4$

Accept that all surgical wounds are inoculated

Risk Reduction

Infection Prevention - Proven

- Prophylactic antibiotics
  - administer 30 minutes before skin incision
  - continue for 24 hours after surgery
- Particle reduction
  - vertical flow systems are superior

Risk Reduction

Infection Prevention - Proven

- Ultraviolet light deactivation
- Antibiotic impregnated cement
  - revisions
  - higher risk patients

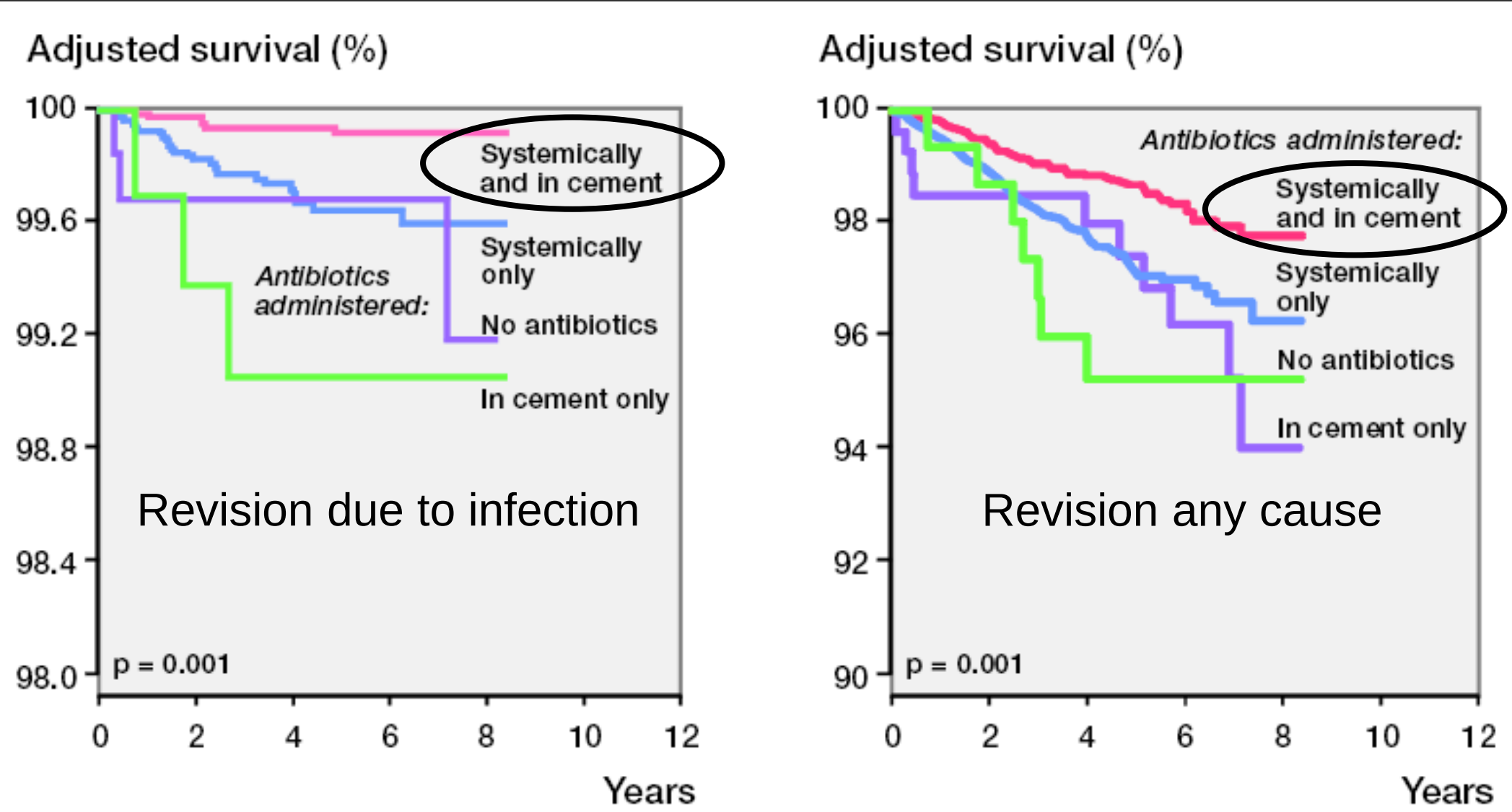


Figure 8. Cox regression-adjusted survival curves of THRs performed in Norway from 1987 to 1995. The probabilities of survival were calculated with revisions due to infection (left) and revision due to any cause (right) as end-points for patients receiving various antibiotic regimens for prophylaxis. The p-values refer to a test for homogeneity showing statistical significant differences in survival among the regimens. The figure is reproduced from Espehaug et al. 1997a, with permission from the Journal of Bone and Joint Surgery (Br).

Current ALAC Protocol

TJA Procedures

- Abx in PMMA - all revision cases
  - Palacos or Cobalt cement
  - no more than 1 gm per 40g bag
    - mechanical properties are decreased by approximately 10%

We All Agree

Biofilm

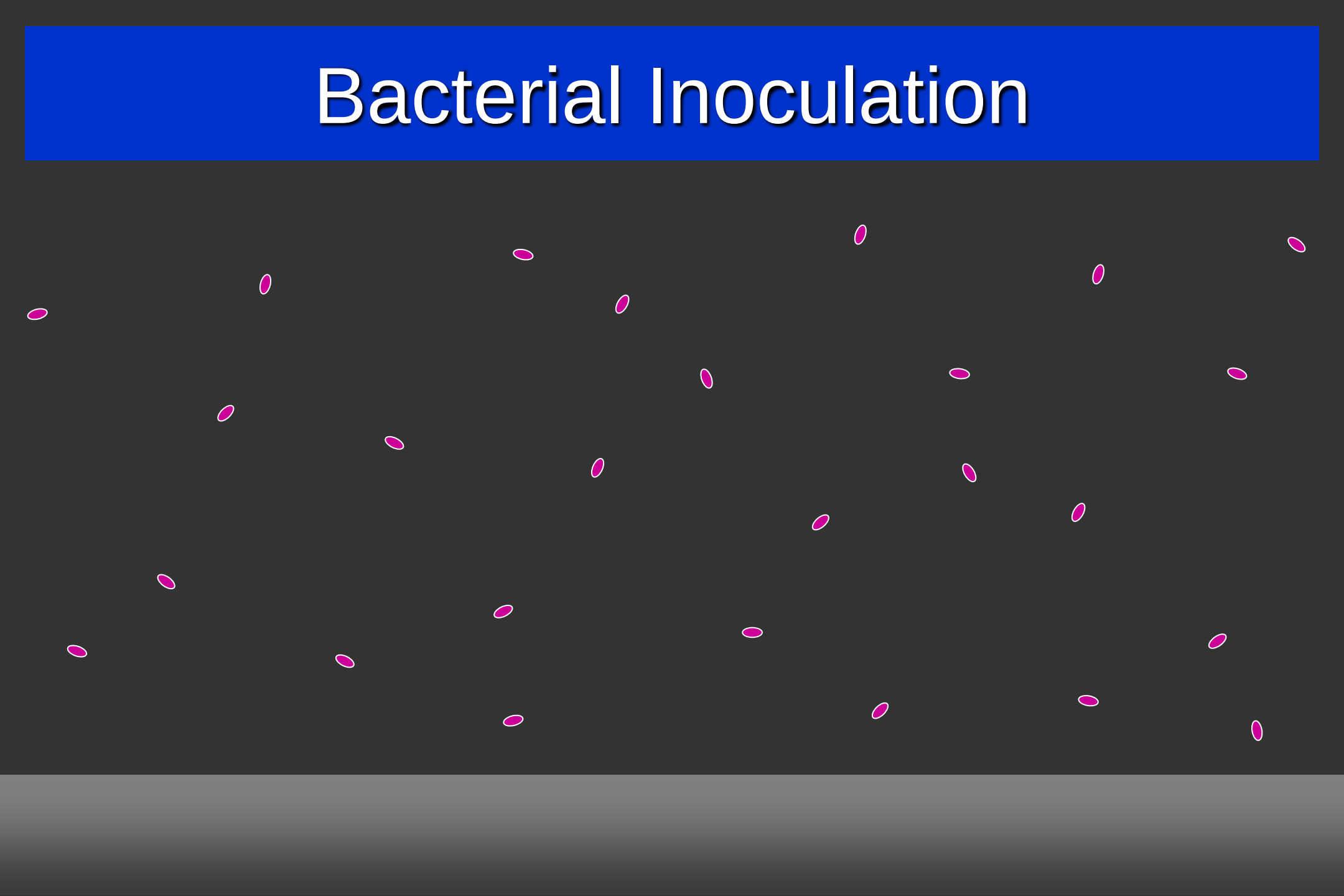
- Biofilm on implants is the cause of chronic disease
- Biofilm prevention - goal
  - quorum deterrence is the method

Biofilm

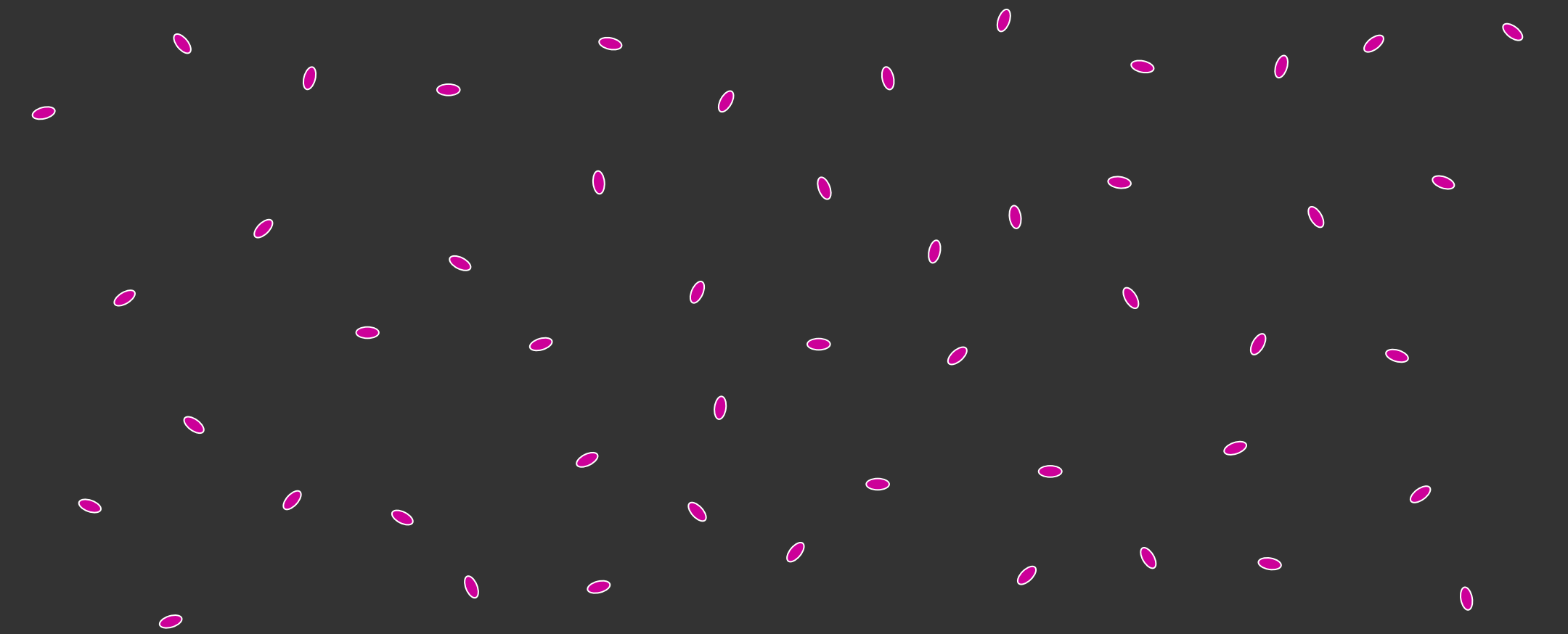
Human Infection

- All bacteria make biofilm
- Biofilm forms on
  - foreign material
  - devitalized tissue

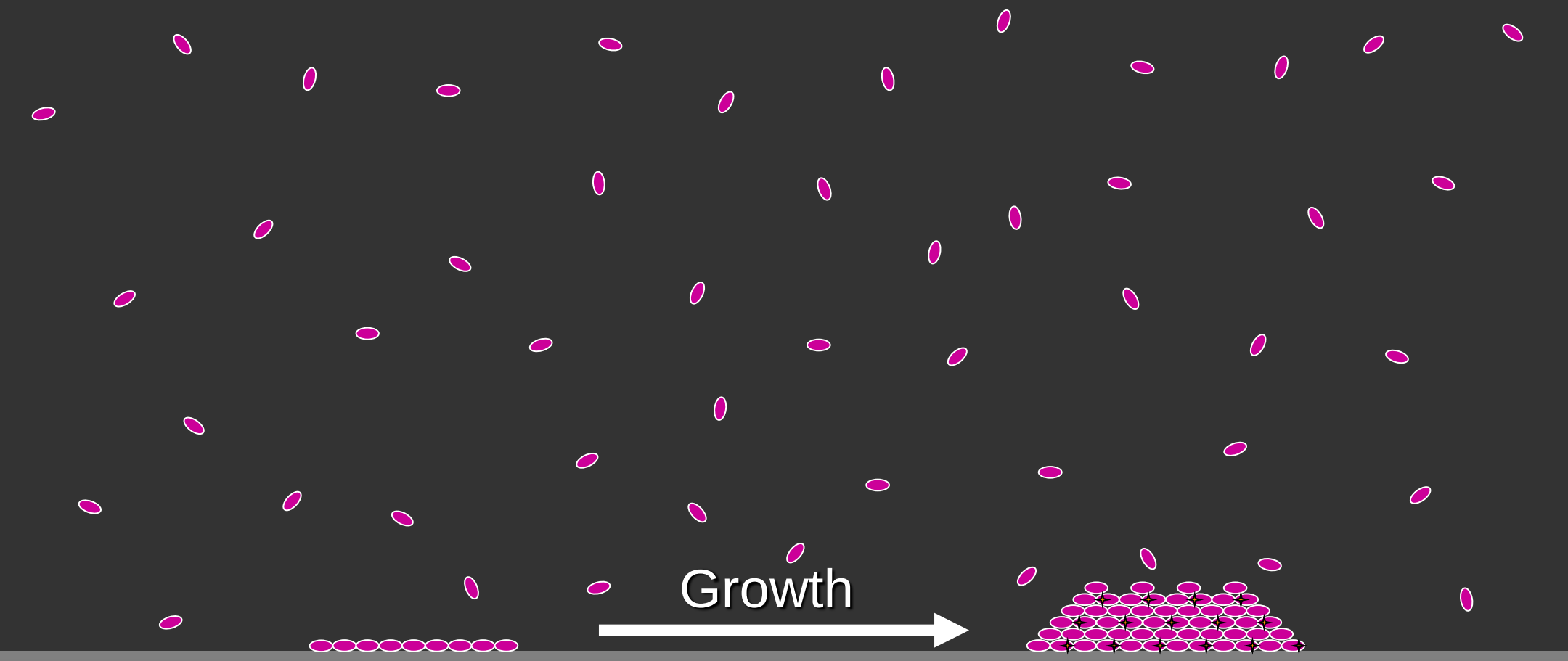
Bacterial Inoculation



Planktonic Multiplication

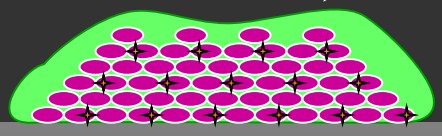


Bacterial Adherence



Biofilm Formation

Polysaccharide Coating

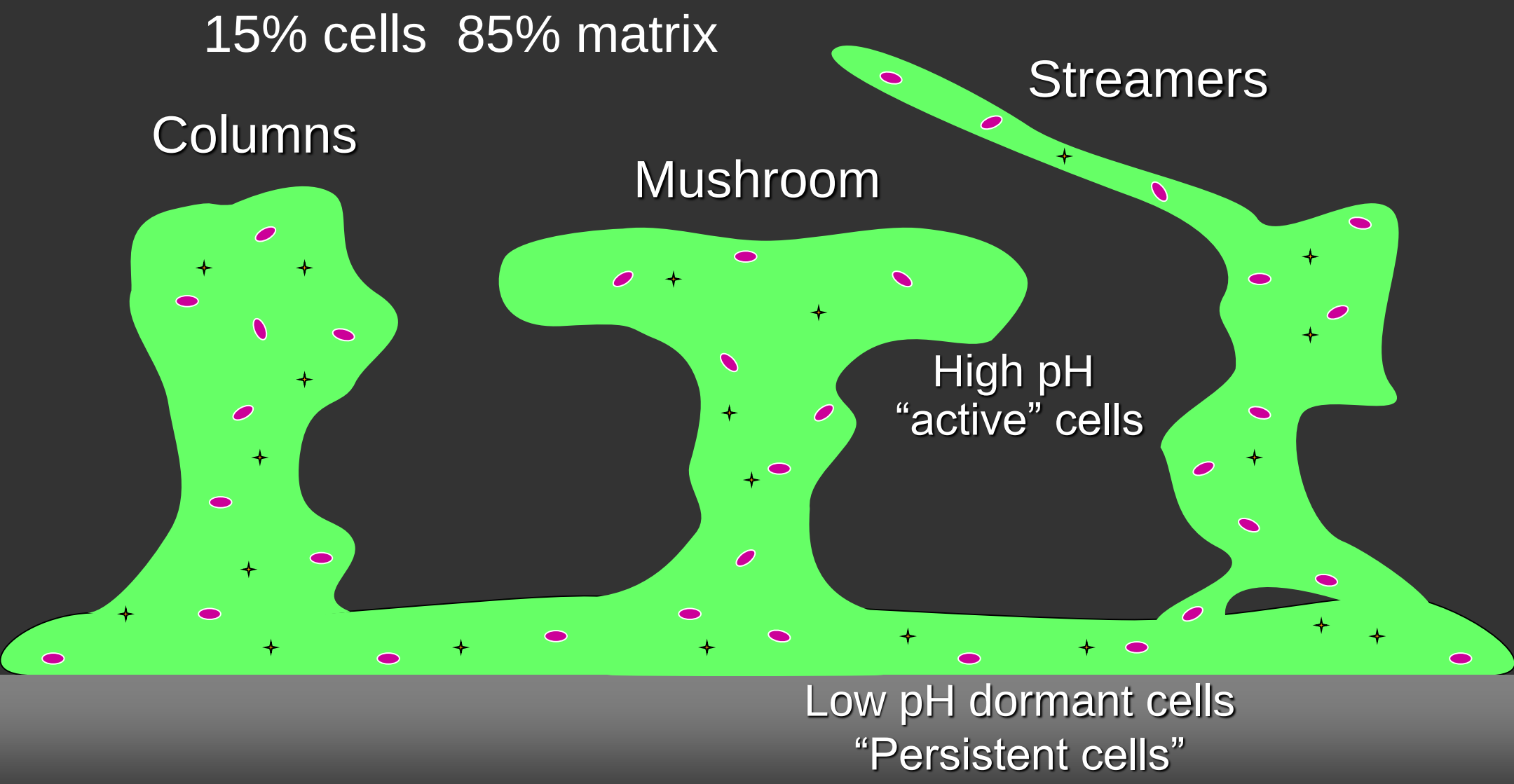


Biofilm Growth

Proliferation
1cm/hr - latex study

Quorum Sensing

Mature Biofilm

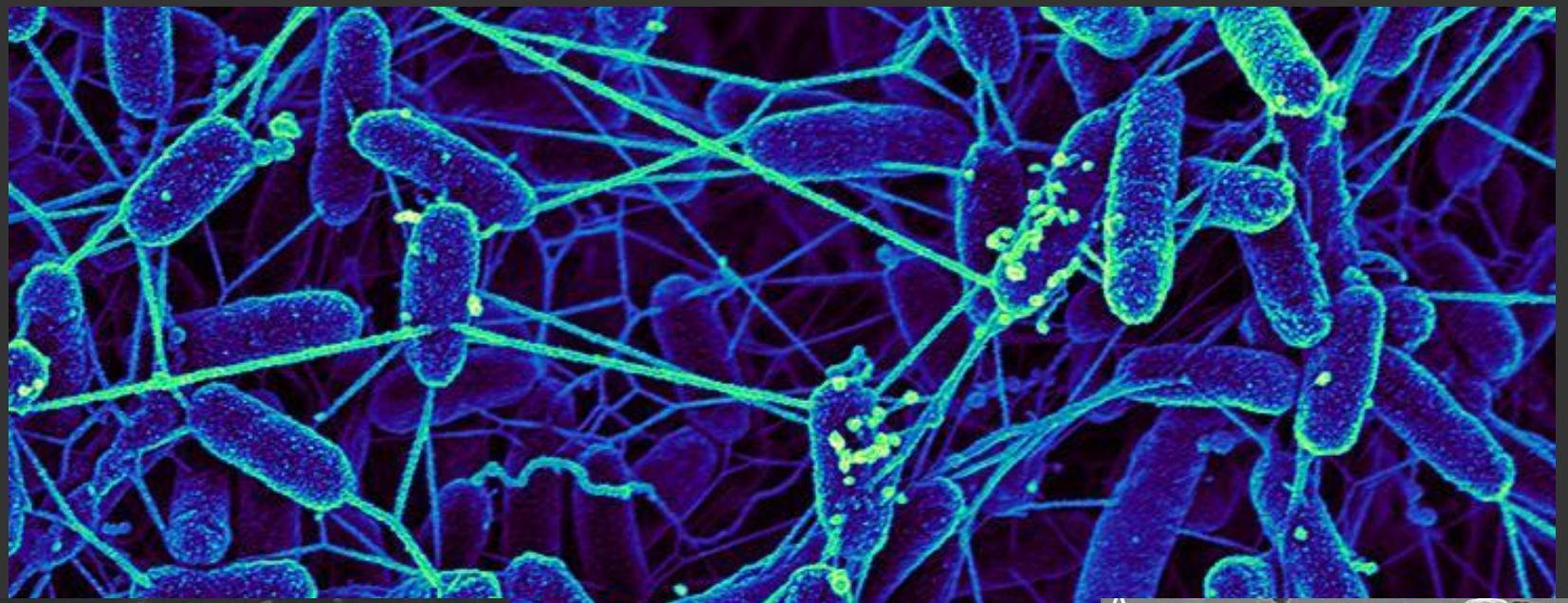


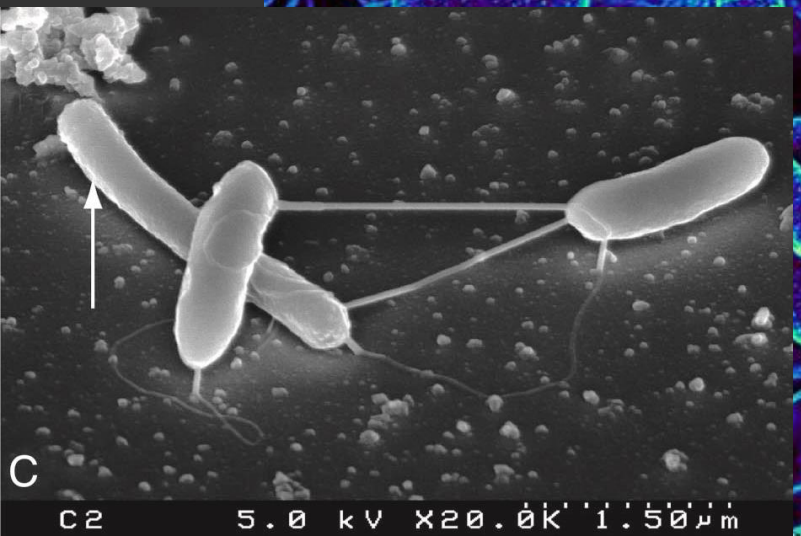
Biofilm State

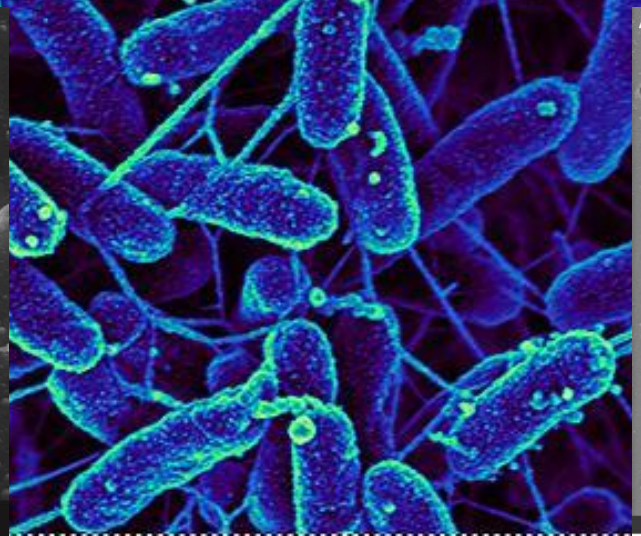
Communication

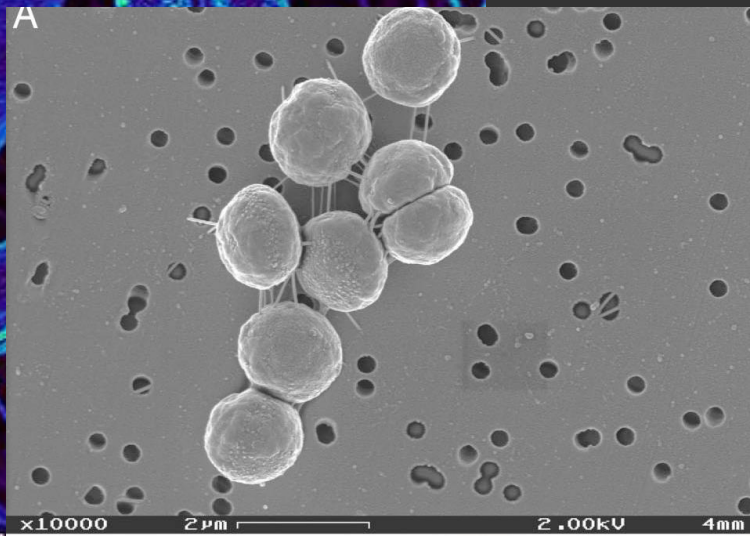
- Molecular transmitters
  - lactone derivatives
- “Nanowires” !!!
  - cell to cell extensions

Biofilm Nanowires









Biofilm State

Significance

- Bacteria become 1000-1500x more resistant to antibiotics
  - bacteria express genes which change cell wall and/or membrane structure

Science 284:1318 99’

Biofilm State

Significance

- Biofilm is permeable (not a shield)
  - antibiotics go through to biofilm base with in 90 seconds
- Resistant to wbc's & phagocytosis
- Resistant to antibodies

Science 284:1318 99'

Biofilm State

Significance

- In vivo, biofilm can colonize, grow & cover a surface within 4 to 8 days!
  - this is why I have concern when there is prolonged wound drainage post-op in a total joint patient!

Biofilm State

Significance

- Biofilm can form on a soaked surface with in 45 minutes
  - OR equipment should be kept dry after cleaning
  - Hand wash basins are not to be allowed

Biofilm State

Significance

- Effective treatment for established biofilm infection requires
  - implant & foreign body removal
    - retained implant/cement pieces = retained biofilm → infxn recurrence
    - this includes broken screws & cement fragments left in canals

Biofilm State

Significance

- Effective treatment for established biofilm infection requires
  - extirpation of all devitalized bone & soft tissue
    - inadequate debridement → reason for failure

Periprosthetic Infection

Diagnosis

- International Consensus Meeting of Musculoskeletal Infection Societies
- Defined criteria for pji are clearly estabilished

Periprosthetic Infection

Definite Diagnosis #1

- Draining sinus that communicates to the joint
  - don’t be fooled by sinus that is located far from the joint or is in an unusual location!!!
  - absolute diagnosis

Draining Sinus

Periprosthetic Infection

Definite Diagnosis #2

- A pathogen isolated from culture from two separate fluid or tissue cultures obtained from the affected prosthetic joint

Periprosthetic Infection

Definite Diagnosis #3

- 4 of the following 6 criteria
  - elevated esr or crp
  - elevated synovial wbc count
    - acute ≥ 20,000 wbc/mm^3
    - chronic ≥ 2500 wbc/mm^3

Periprosthetic Infection

Definite Diagnosis #3

- 4 of the following 6 criteria
  - elevated synovial neutrophil (pmn) percentage
    - acute ≥ 89% neutrophils
    - chronic ≥ 70% neutrophils

Periprosthetic Infection

Definite Diagnosis #3

- 4 of the following 6 criteria
  - isolation of a pathogen in one culture from fluid or tissue obtained from the affected joint
    - remember cx's can be negative
  - presence of purulence in the affected prosthetic joint

Periprosthetic Infection

Definite Diagnosis #3

- 4 of the following 6 criteria
  - >5 neutrophils per high power field in 5 high power fields observed from histologic review of periprosthetic tissue at 400x magnification

Periprosthetic Infection

Be Very Suspicious

- Spontaneous onset of wound drainage in a previously dry perioperative surgical wound

Treatment

Type I & II - Acute

- Open I&D, lavage
  - component retention
  - modular bearing change
- Consider resection in C host

Treatment

Type I & II - Acute

- IV antibiotics 6 weeks
  - oral antibiotics for another 6 weeks is ok
- Follow wsr, crp & exam
- Recurrence → chronic
  - biofilm state

Treatment

Type III - Biofilm State

- Implant resection
- Radical debridement
  - “tumoresque” removal of tissue
- Joint stabilization

Treatment

Type III - Biofilm State

- IV antibiotics for 6 weeks
- Re-evaluation - off antibiotics for 2 weeks
  - clinical exam
  - cbc, wsr, crp
  - aspiration studies & x-rays

Treatment

Type III - Biofilm State

- Definitive treatment
  - reimplantation
  - permanent resection
  - arthrodesis
  - disarticulation

Antibiotic Loaded PMMA Spacers

Rationale

- Antibiotic delivery
  - delivery to local site at high concentrations
  - not biofilm killing doses
- Dead space obliteration

Antibiotic Loaded PMMA Spacers

Functional Spacers

Antibiotic Loaded PMMA Spacers

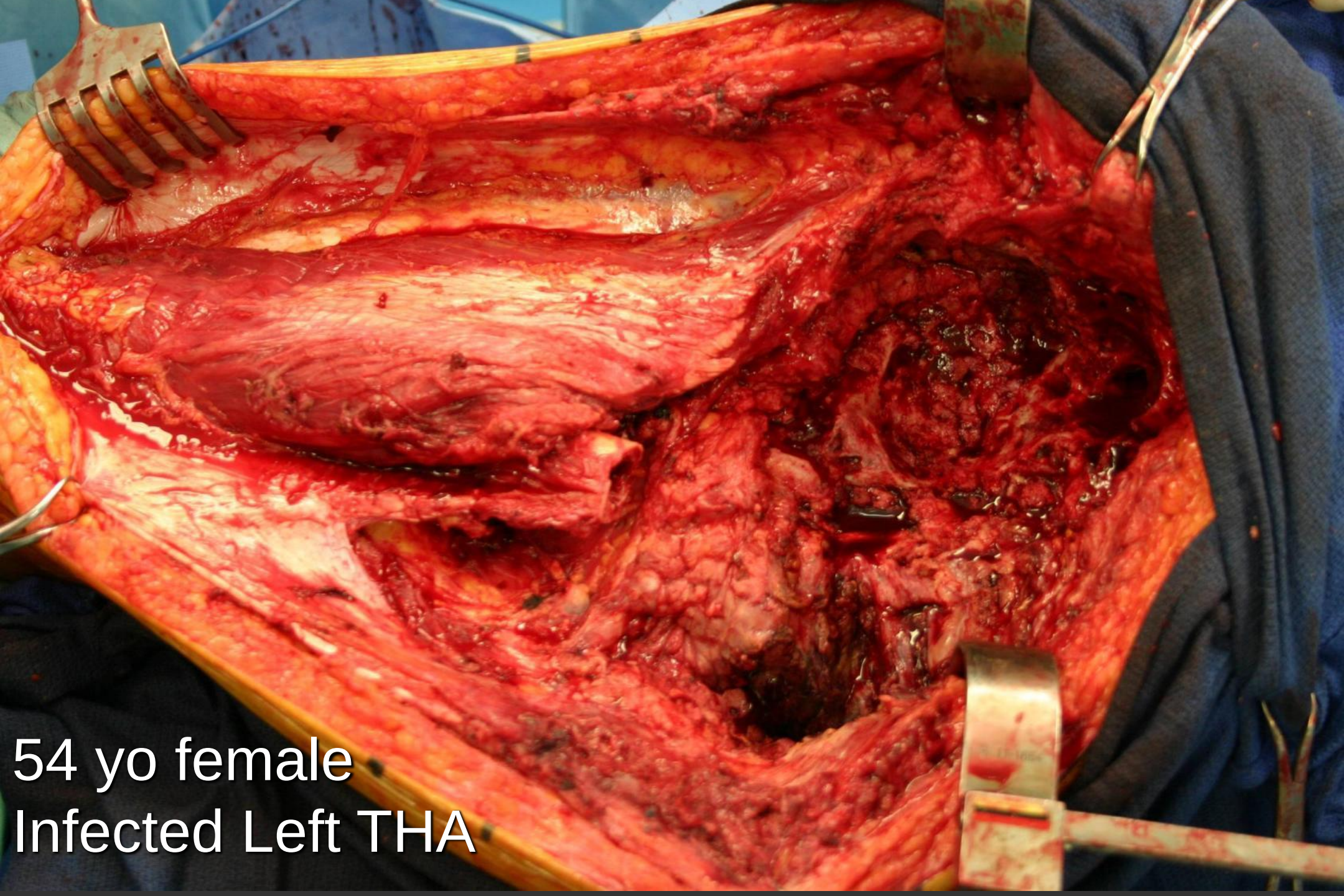
My Current Formula*

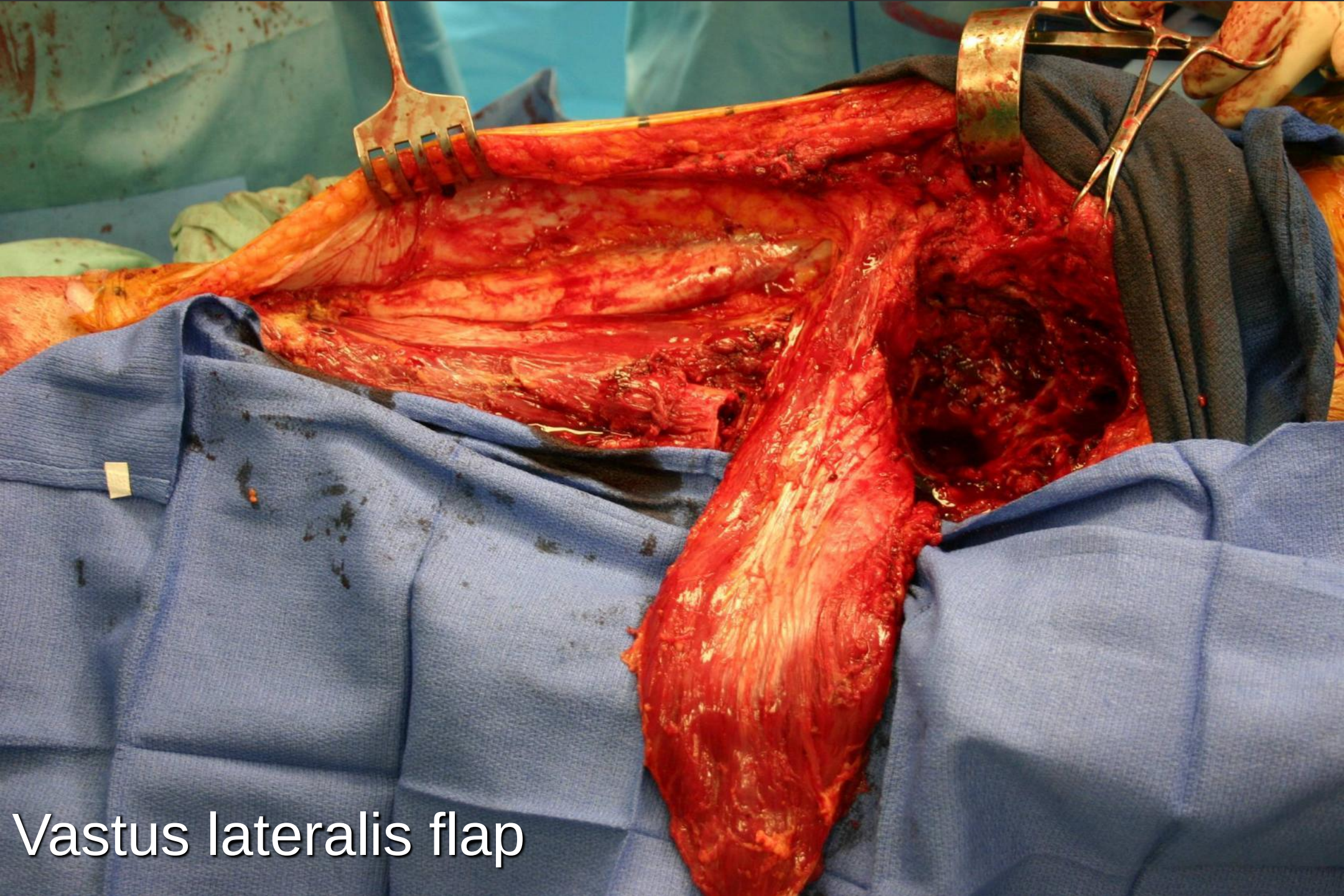
- Cement
  - cobalt or palacos
- Per 40 gm bag of cement powder
  - 5.0 gm vancomycin
  - 3.6 gm tobramycin

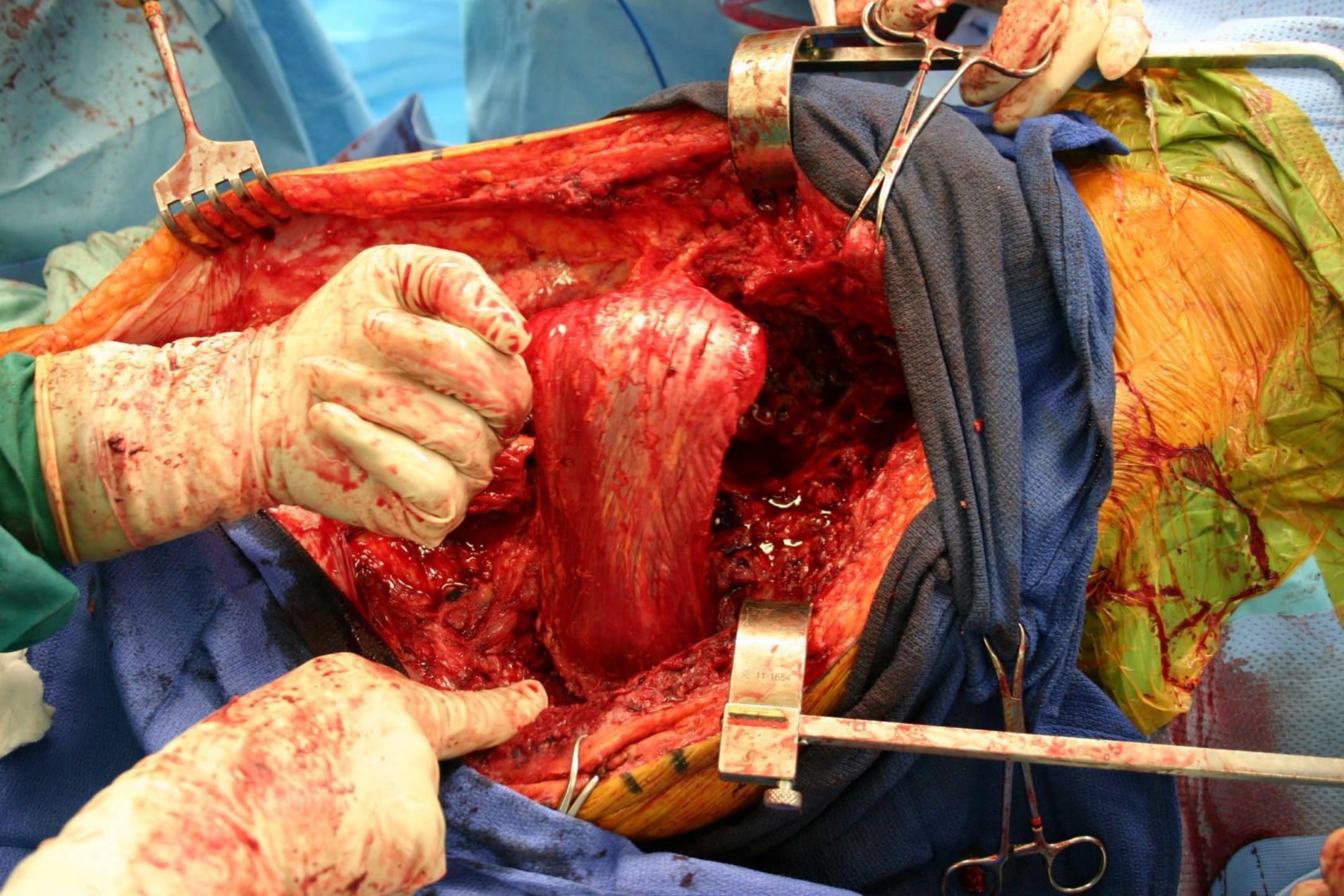
Reimplantation

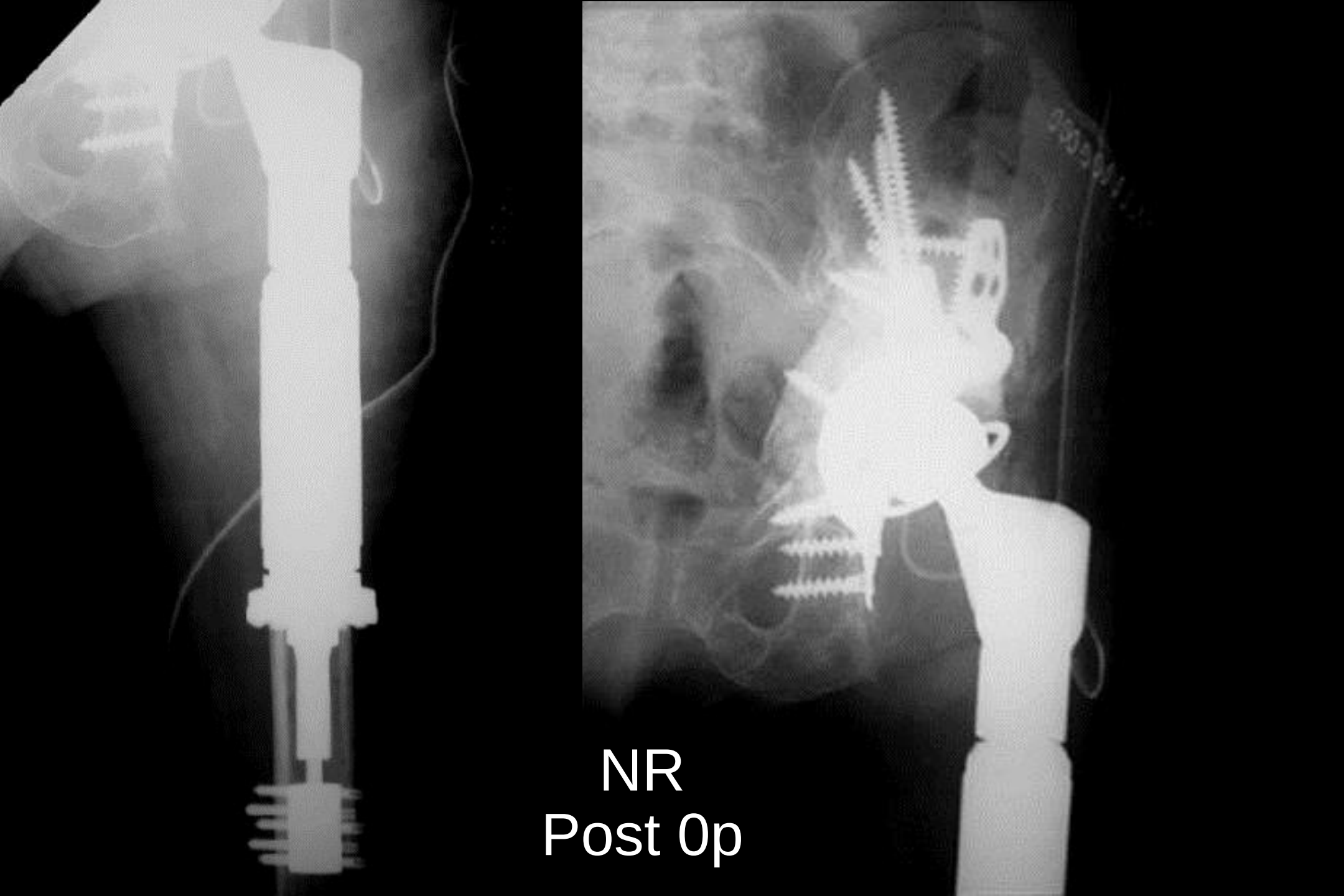
My Trends

- Shift away from bulk allografts
  - difficult to treat if recolonized
- Fill defects with metal
  - extended porous surfaces
  - custom implants helpful

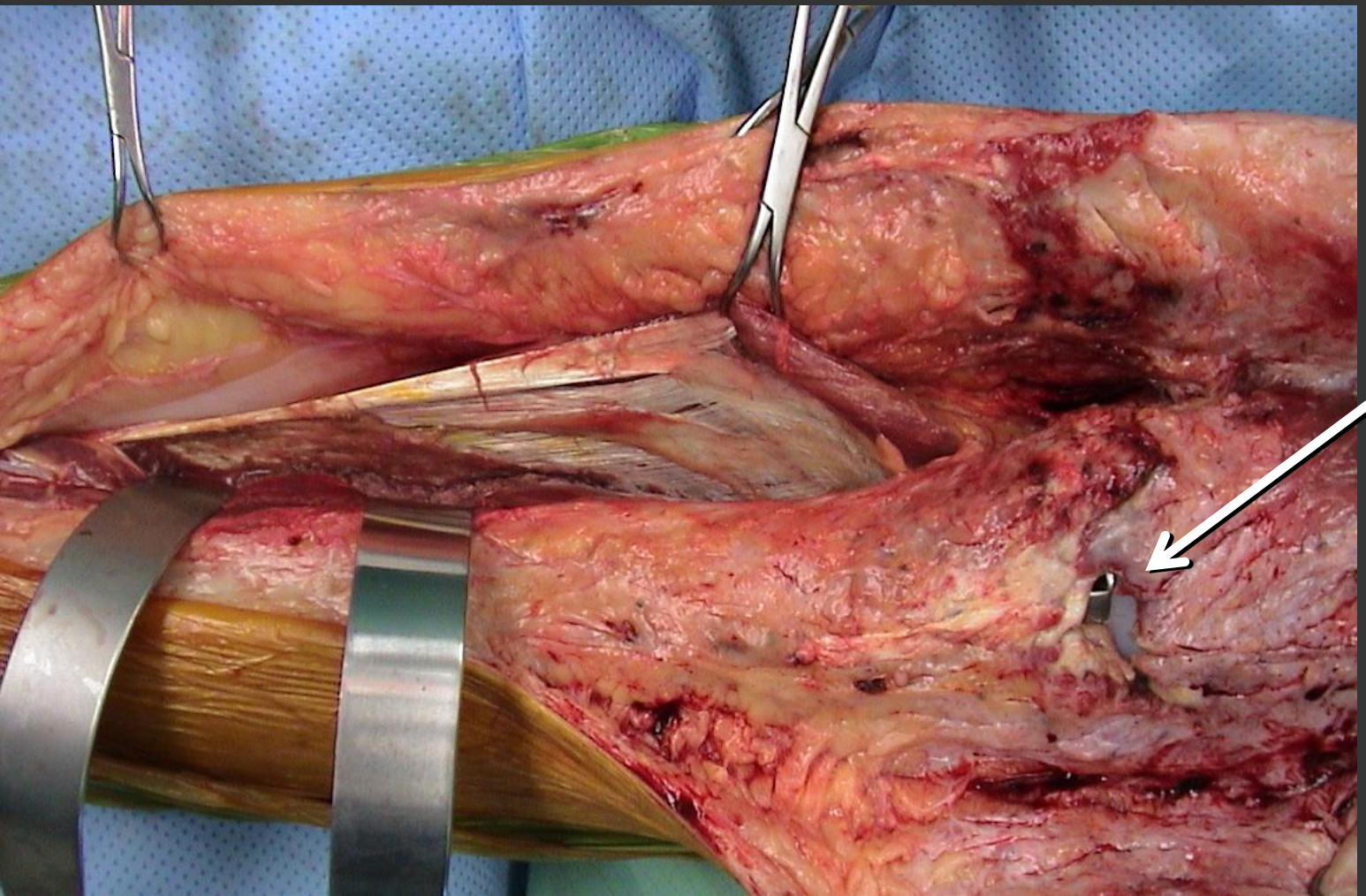

54 yo female
Infected Left THA


Vastus lateralis flap



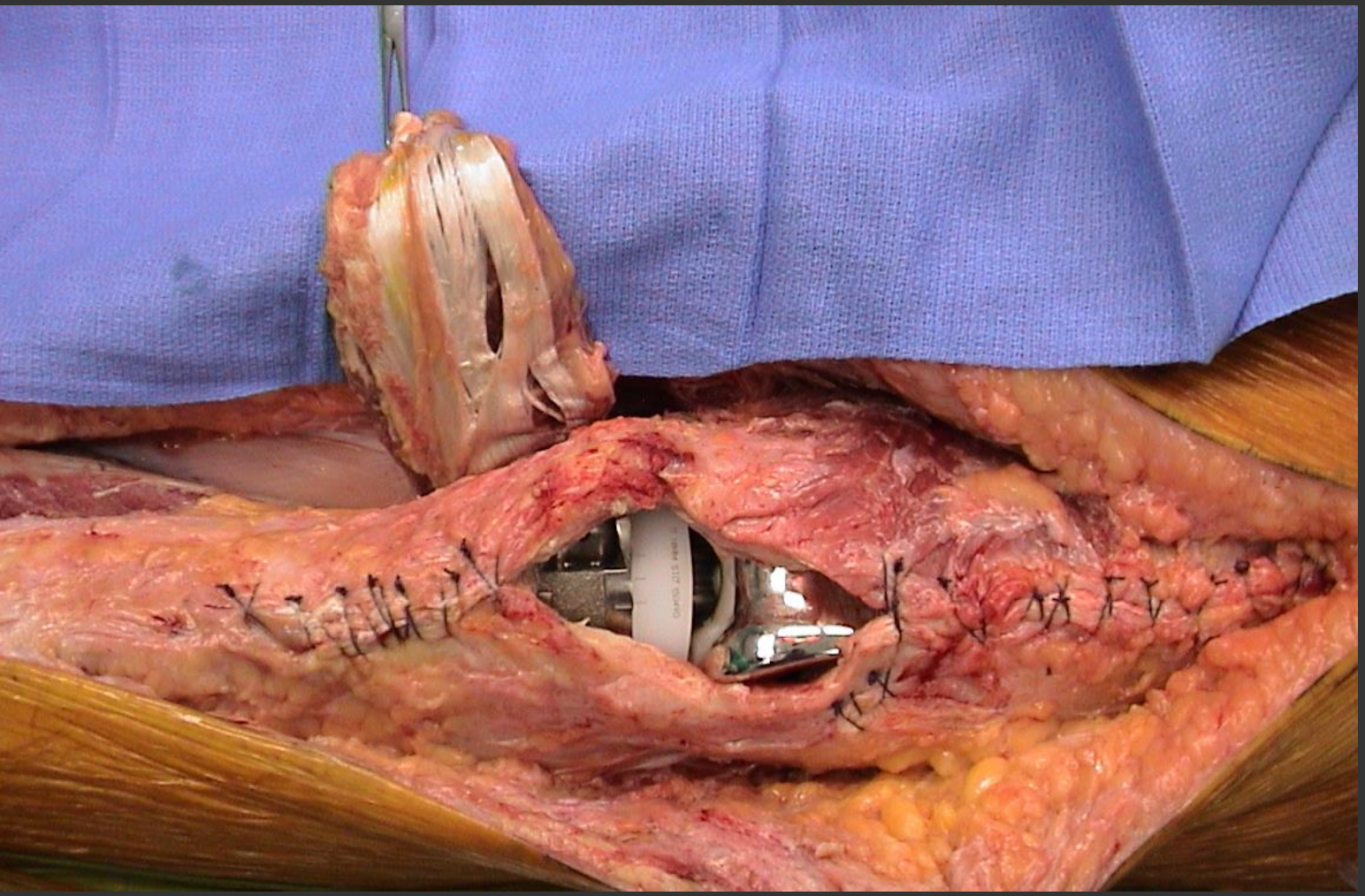

NR
Post 0p

Medial Gastroc Rotation



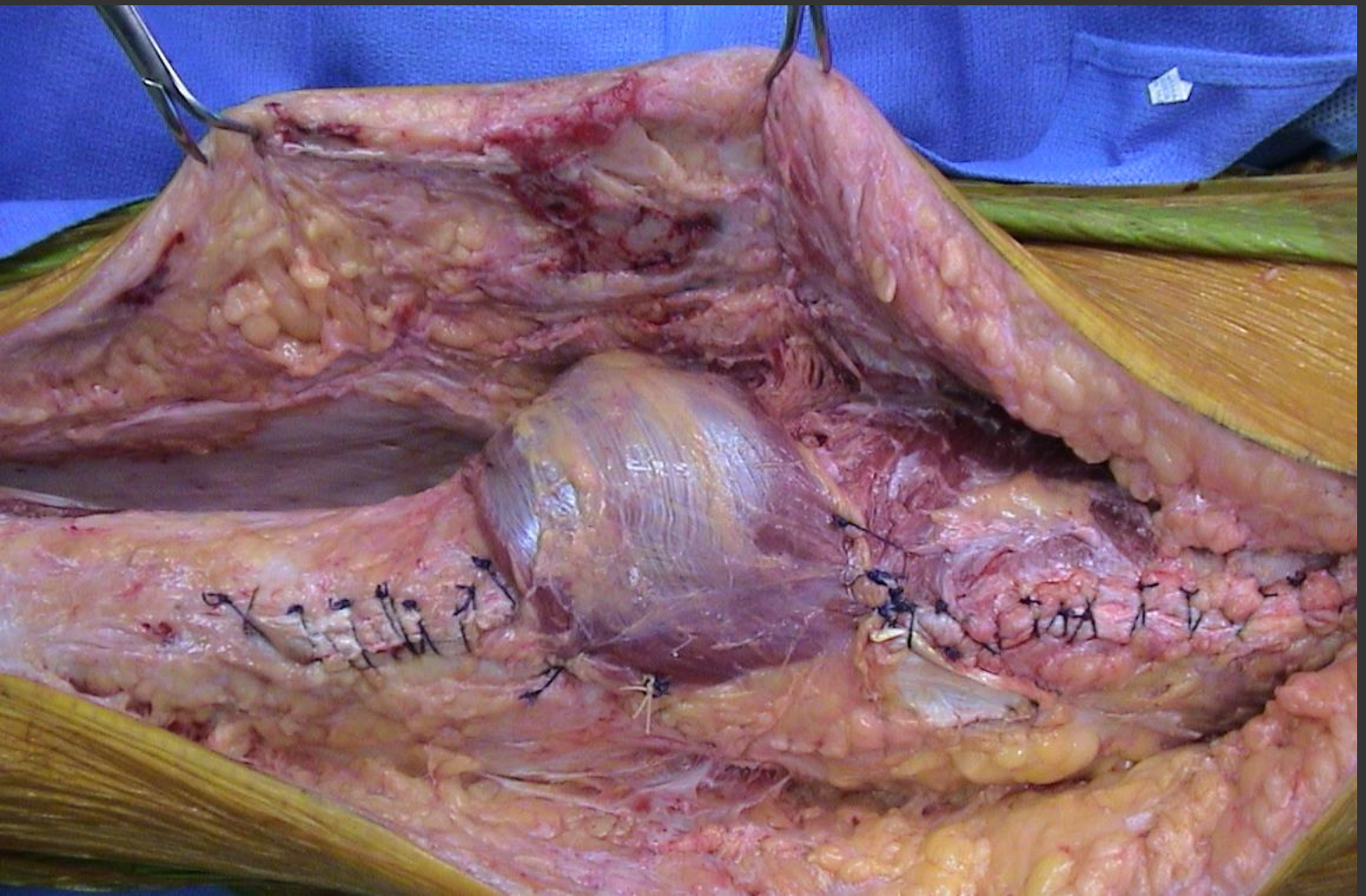
Anterior knee deficiency with drainage

Medial Gastroc Rotation



Anterior knee deficiency after debridement

Medial Gastroc Rotation



Anterior knee deficiency covered with flap

Calcium Sulfate

Clinical Use - Orthopaedics

- Gypsum
  - mined & processed
  - many products
- Stimulan
  - pharmaceutical grade - synthesized
  - physiologic pH

Calcium Sulfate

My View

- I have used calcium sulfate since the mid 90's
- I continue to use calcium sulfate as a tool to manage bacterial colonization and pji management
  - this is my current research

CP $CaSO_4$

Intra-Articular Beads

- Good intra-articular abx levels
- Potential biofilm bactericidal levels
  - bench studies show potential

Local delivery is better than systemic delivery

CP $CaSO_4$

Intra-Articular Beads - Elution

Mean Local Antibiotic Levels		
Postoperative Day	Vancomycin (µg/mL)	Tobramycin (µg/mL)
1	265	31
2	172	9.4
3	146	6.4
4	146	5.3
5	104	4.6

Maale G: AAOS 2.11.12 San Francisco

Infection Treatment

Microbial MIC's

Pathogen	Antibiotic	MIC_{90} µg/ml	Reference
MRSA	Amikacin	32	[3]
MRSA	Daptomycin	0.78	[2]
MRSA	Fusidic Acid	0.5	[1]
MRSA	Moxifloxacin	0.5	[10]
MRSA	Vancomycin	1	[3]
MSSA	Vancomycin	1	[5]
Enterococcus faecalis	Ampicillin	4	[12]
Enterococcus faecalis	Linezolid	4	[12]
Enterococcus faecalis	Vancomycin	4	[12]
Enterococcus faecium	Ampicillin	128	[12]
Enterococcus faecium	Linezolid	4	[12]
Enterococcus faecium	Vancomycin	4	[12]
Staphylococcus aureus	Daptomycin	0.15	[13]
Staphylococcus aureus	Daptomycin	0.5	[14]
Staphylococcus aureus	Vancomycin	0.1	[11]
Staphylococcus aureus	Gentamicin	0.1	[11]
Staphylococcus aureus	Gentamicin	1	[7]
Staphylococcus aureus	Erythromycin	8	[8]
Staphylococcus aureus	Tetracycline	4	[6]
Staphylococcus epidermidis	Daptomycin	0.31	[13]
Staphylococcus epidermidis	Gentamicin	0.125	[7]
Staphylococcus epidermidis	Vancomycin	2	[4]

Multiple

CP $CaSO_4$

Intra-Articular Beads

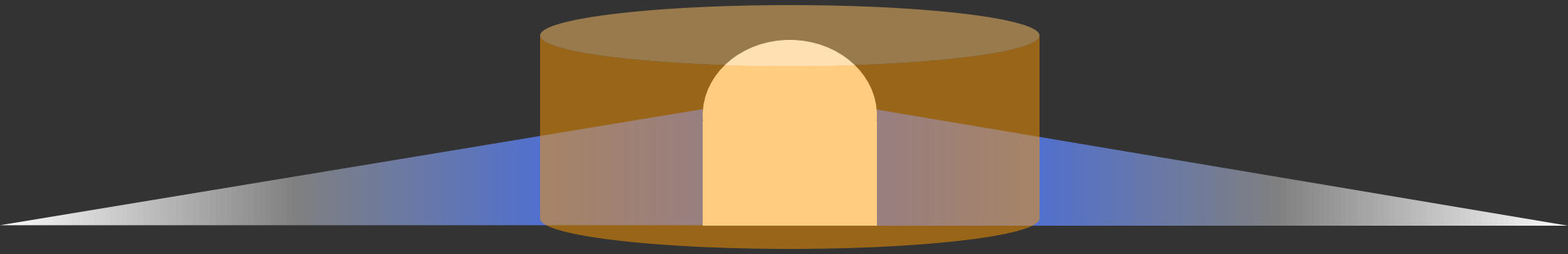
- Biofilm killing potential with both MRSA & Staph Epi
  - logrithmic reduction but not complete
  - thus, debridement plays concomitant role in treatment

Stoodley P: Antimicrob Agents & Chemo 59:1:111 15'

Biofilm Eradication

Local Delivery To AOI

Biofilm Kill Zone



? The More the Merrier ?

Calcium Sulfate

Wound Leaks - Etiology?

- Impurities
- Osmolality
- Poor technique - tissue trauma
- Poor tissues
- Overstuffing

Lee GH et al: Iowa Orth J. 22:35 02’

Calcium Sulfate

Wound Leaks - Observations

- Better than gypsum product
- Overstuffing affects leak rate
- Poor tissues = poor healing
  - less beads

Sweet Spot 10-30cc (liquid)

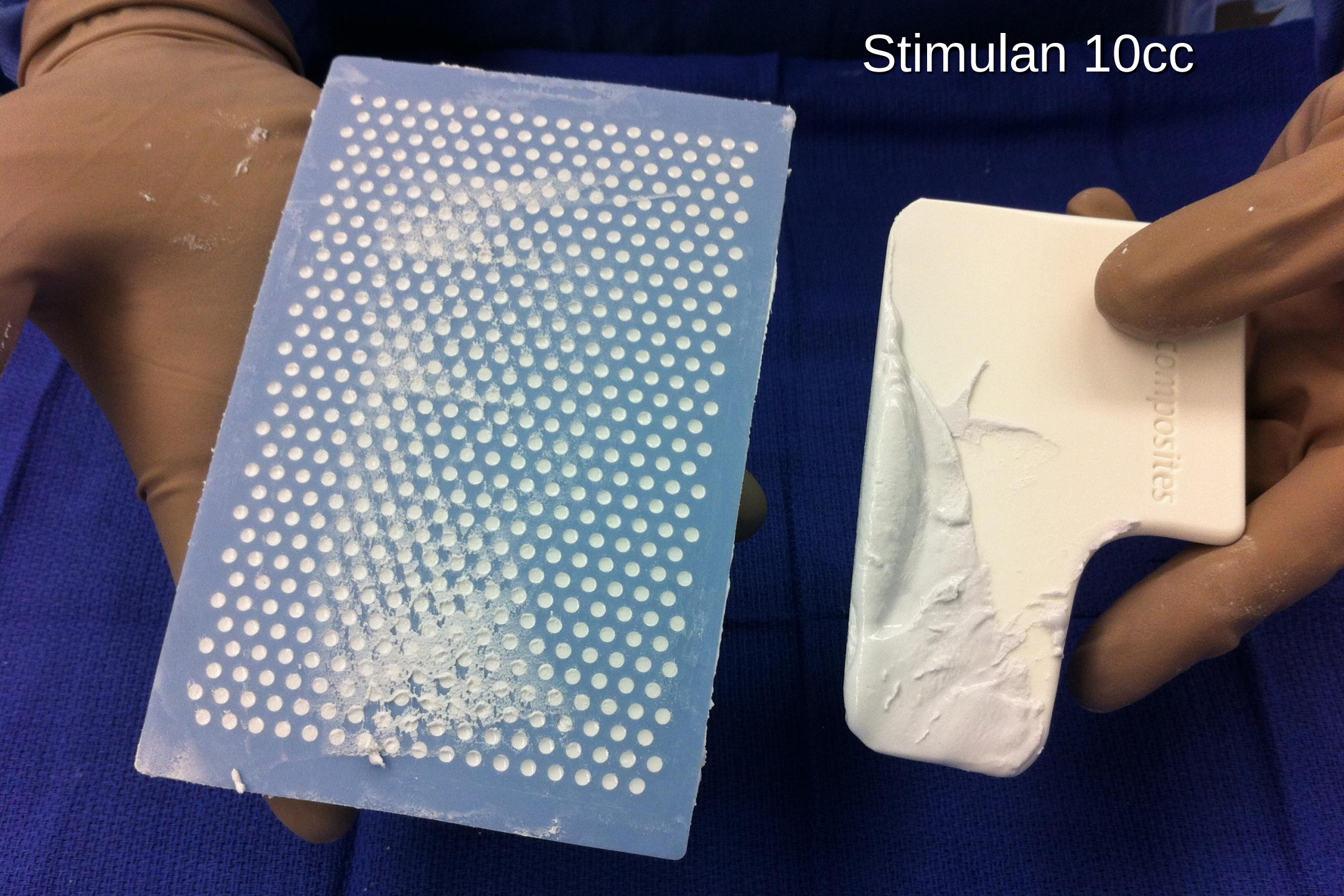
Stimulan Calcium Sulfate

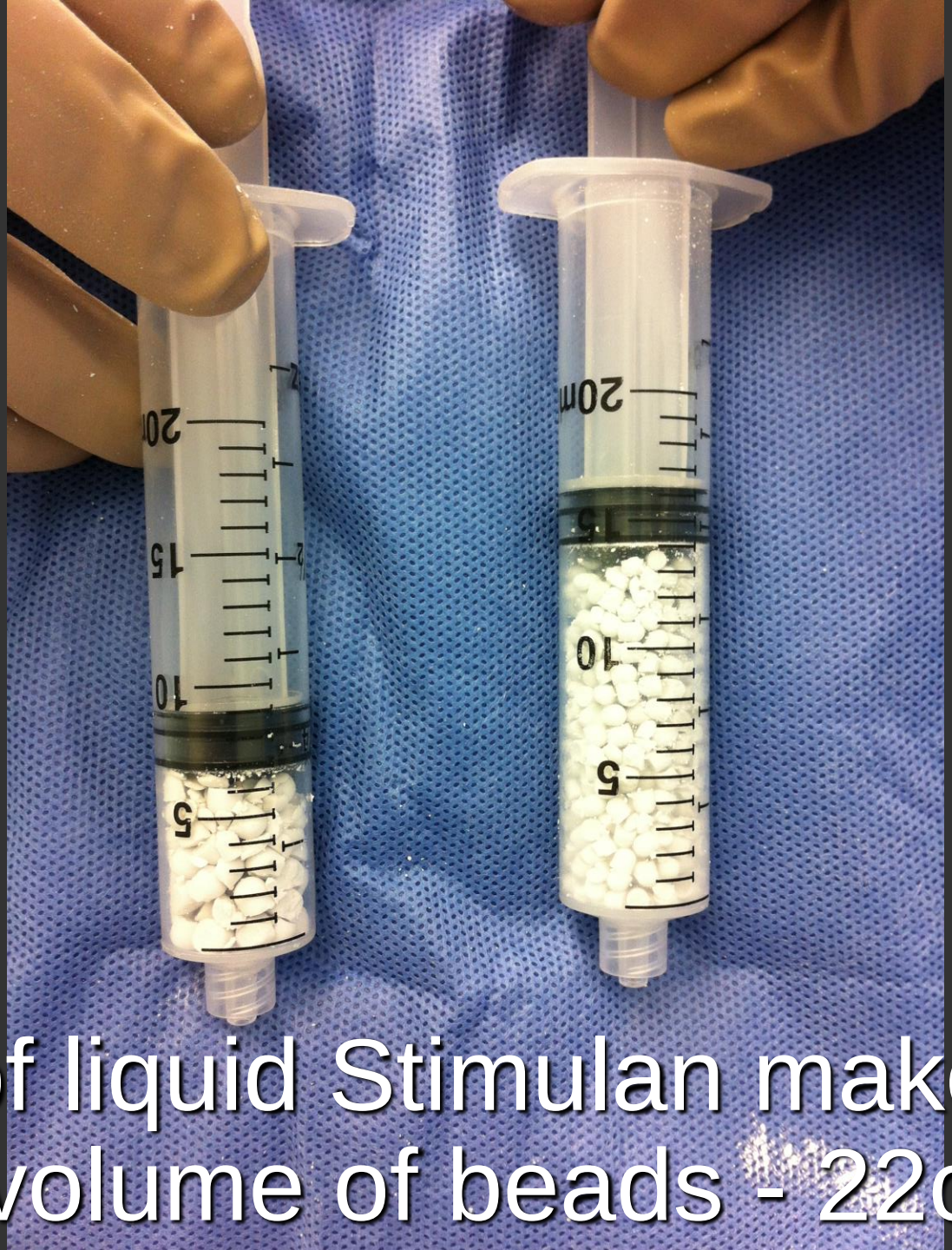
N=250

- Wound drainage 4%
- Heterotopic ossification 1.6%

Current Review
N=610

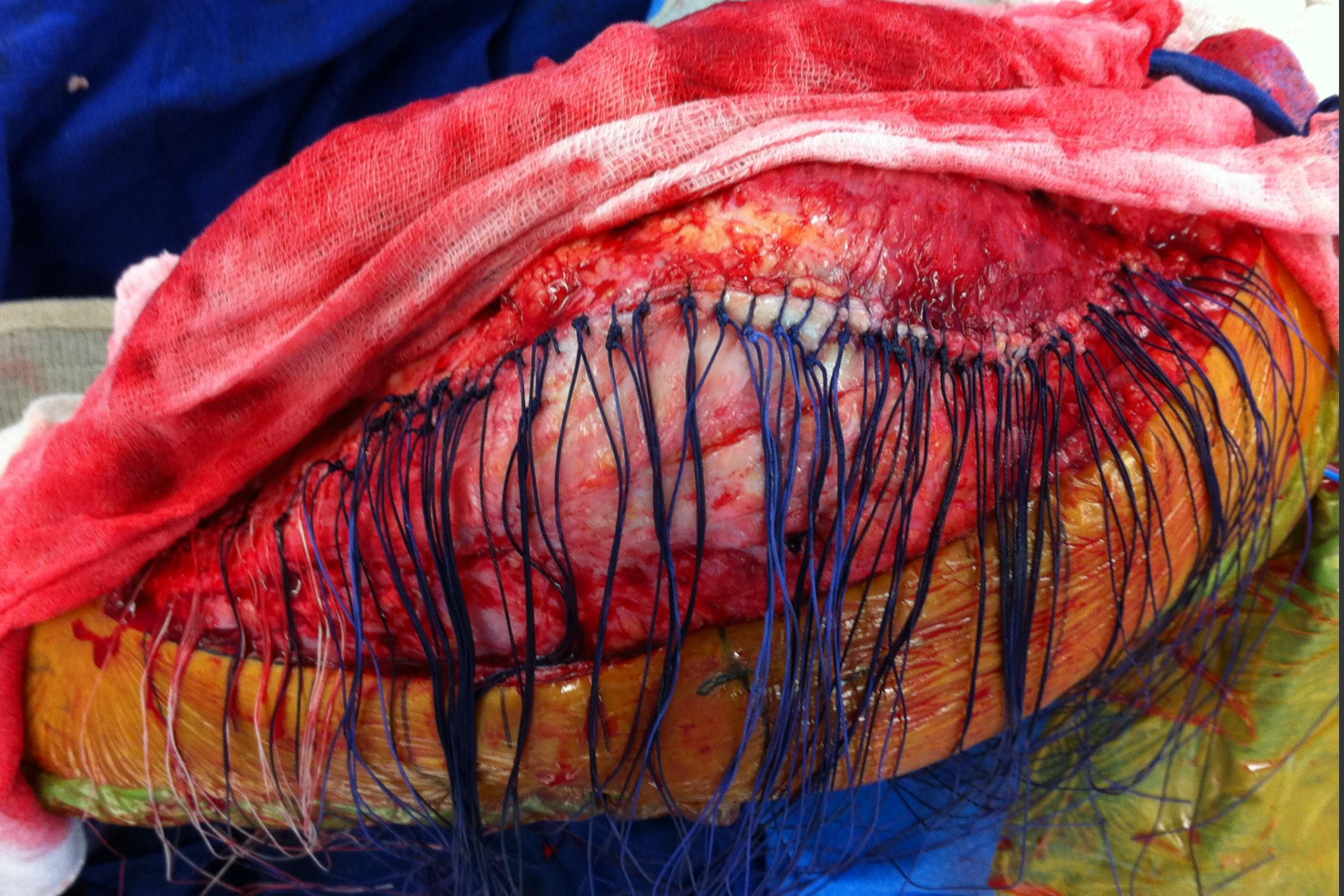
McPherson EJ, Sherif SM: J.Recon Review 2:1 13’


Stimulan 10cc



10cc of liquid Stimulan makes this volume of beads - 22cc

Drains



Stimulan Calcium Sulfate

Aseptic Revision TKA
N=177

- Avg Stimulan/case 14cc
- Range 5-40
- Complications 25
- Failures 10
- Infxn failures 2
- Drainage 4

Aseptic Revision THA
N=150

- Avg Stimulan/case 19cc
- Range 5-50
- Complications 9
- Failures 8
- Infxn failures 3
- Drainage 3

Last Review 2.18.15

Stimulan Calcium Sulfate

DECRA TKA
N=31

- Avg Stimulan/case 23cc
- Range 10-40
- Complications 4
- Failures 4
- Infxn failures 3
- Drainage 2

DECRA THA
N=15

- Avg Stimulan/case 36cc
- Range 10-60
- Complications 1
- Failures 1
- Infxn failures 1
- Drainage 1

Stimulan Calcium Sulfate

Resection TKA
N=82

- Avg Stimulan/case 32cc
- Range 10-80
- Complications 9
- Failures 2
- Infxn failures 1
- Drainage 2

Resection THA
N=49

- Avg Stimulan/case 35cc
- Range 10-60
- Complications 9
- Failures 1
- Infxn failures 1
- Drainage 1

Stimulan Calcium Sulfate

Reimplant TKA
N=65

- Avg Stimulan/case 24cc
- Range 10-40
- Complications 12
- Failures 6
- Infxn failures 5
- Drainage 8

Reimplant THA
N=41

- Avg Stimulan/case 33cc
- Range 10-70
- Complications 4
- Failures 2
- Infxn failures 1
- Drainage 3

Stimulan Calcium Sulfate

N=571

- Wound drainage 4.0%
- Heterotopic ossification 1.2%
- Hypercalcemia 15%

Last Review 3.23.15

Chronic Periprosthetic Infection

Antibiotic Delivery

- Cobalt or Palacos
  - 5.0 gm vancomycin
  - 3.6 gm tobramycin
- Stimulan Beads
  - 1.0 gm vancomycin
  - 240mg tobramycin

Antibiotic Synergy

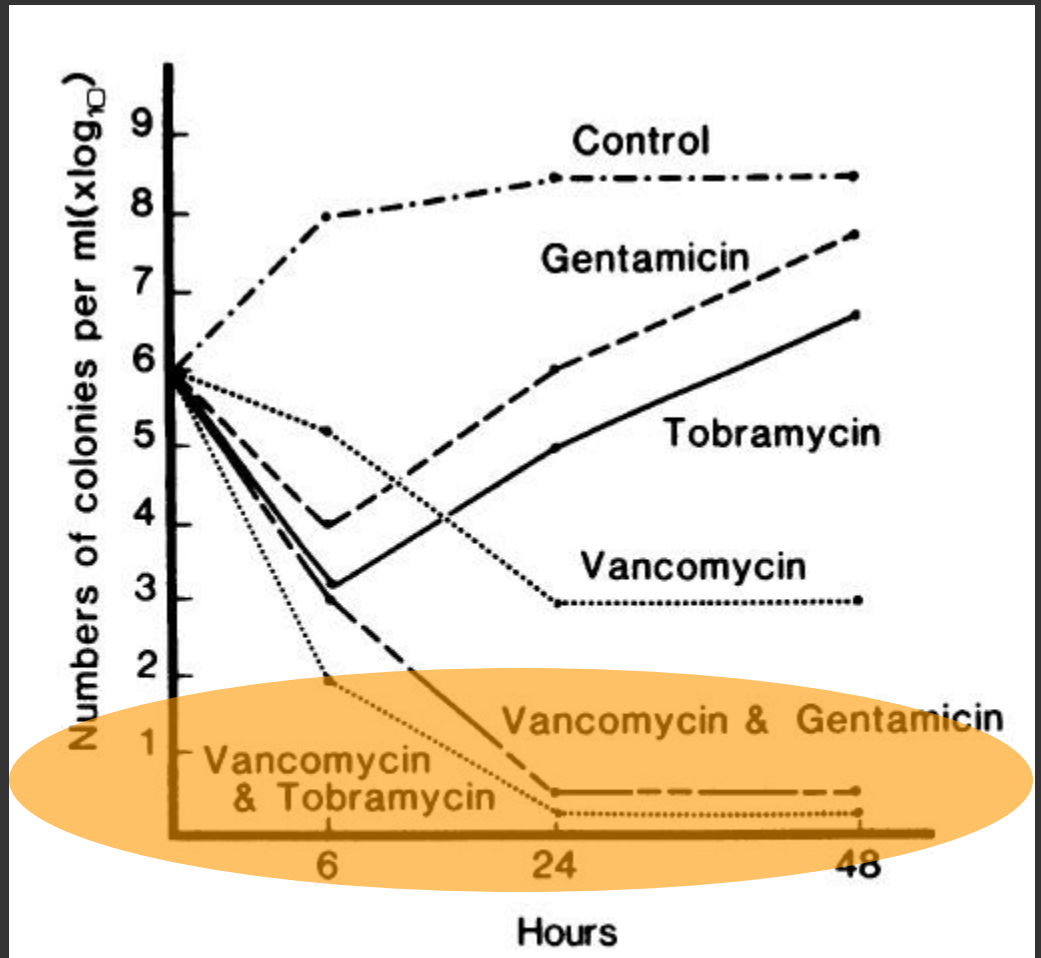


FIG. 1. Time-kill curves of a strain of *S. aureus* showing synergism between vancomycin and gentamicin and between vancomycin and tobramycin.

Watanakunakorn C. Tisone JC
Antimicrob Agents &
Chemoherapy 22:5 903 82'

CP $CaSO_4$

How I Have Changed

- ALAC to Prostalac
  - stimulan helps prevent biofilm formation
  - I just went for it

CP $CaSO_4$

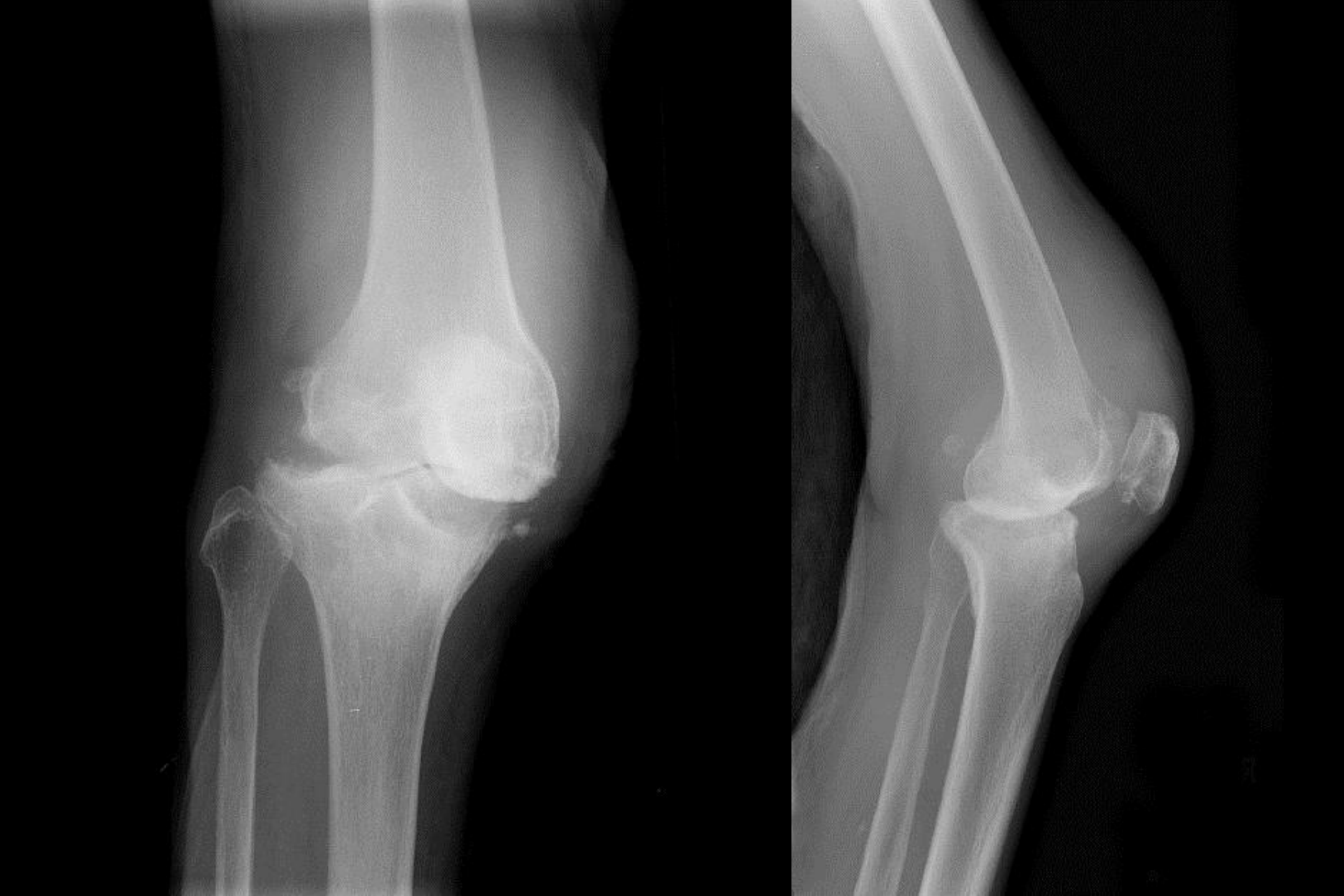
How I Have Changed

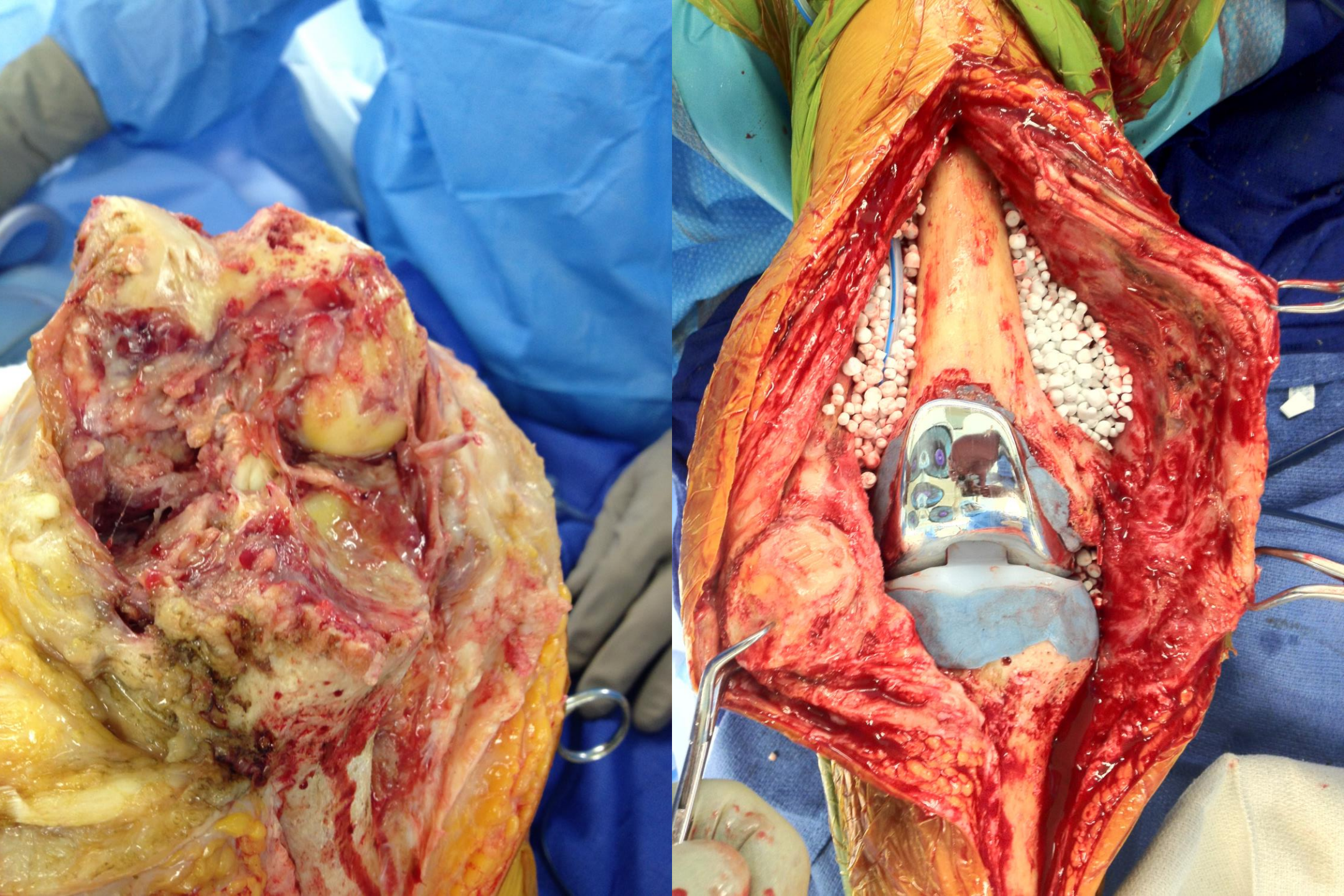
- Coating cementless femoral stems in revision THA
  - a personal goal for me for the last 8 years
  - early data supports that it is protective like abx pmma

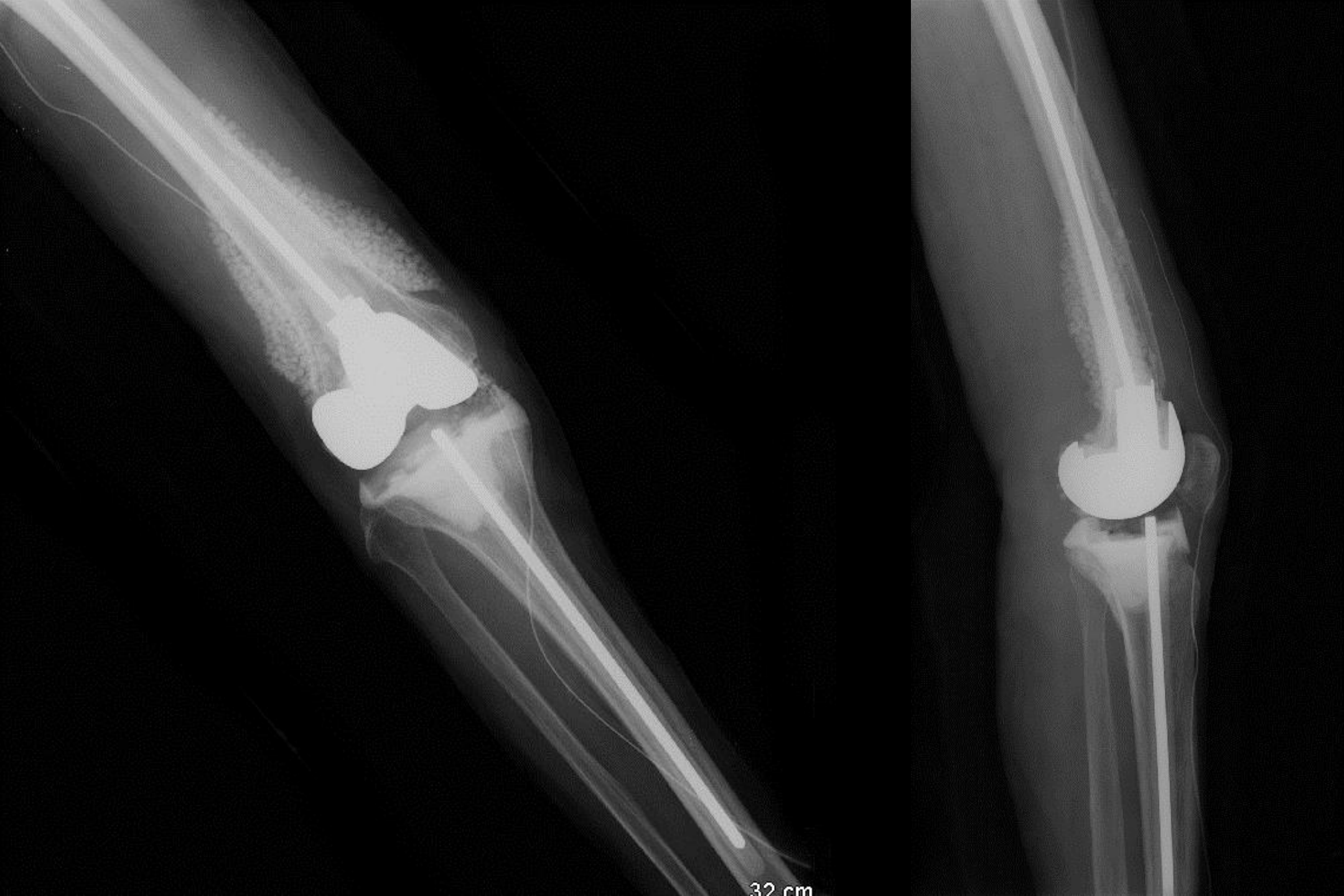
CP $CaSO_4$

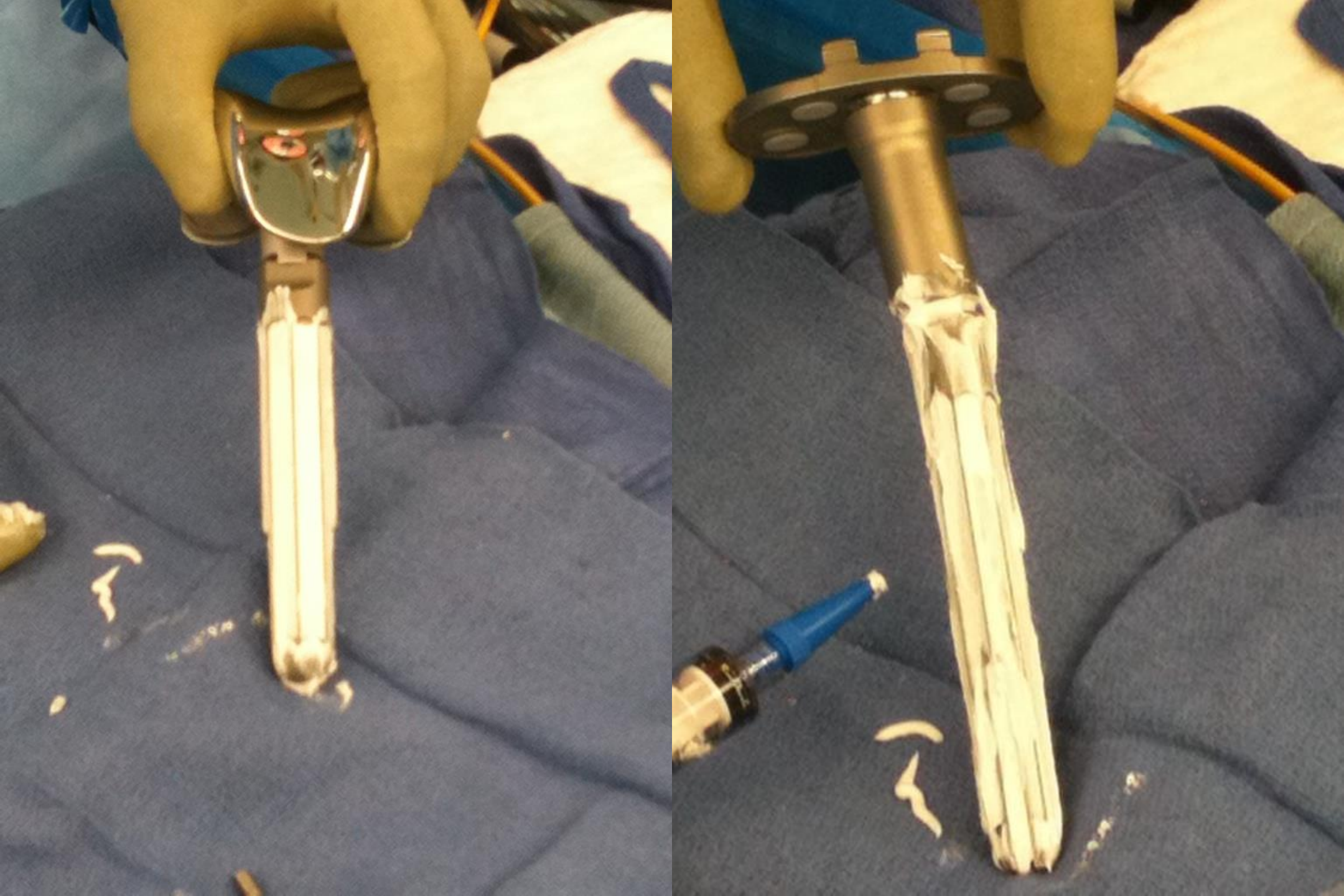
How I Have Changed

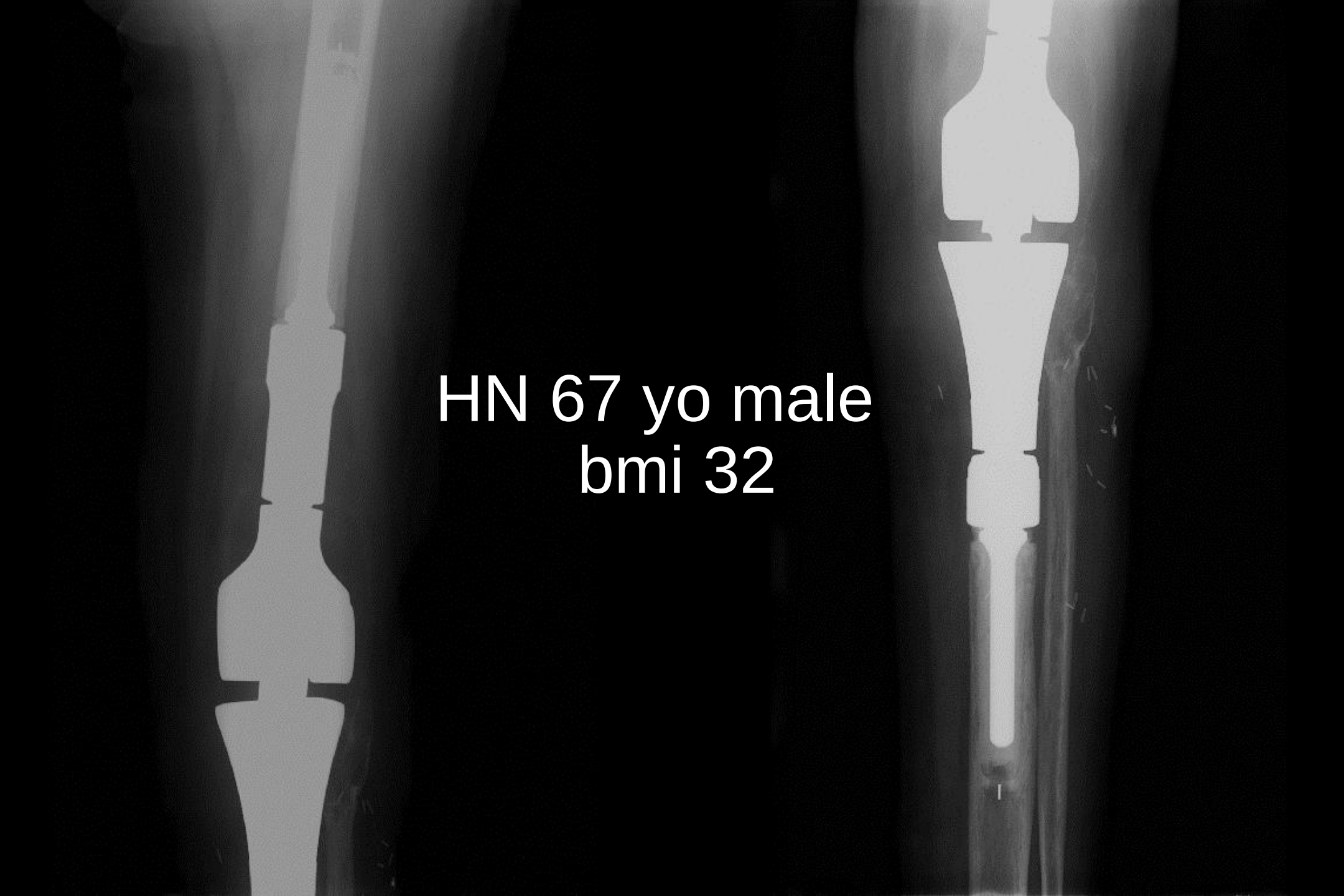
- Coating stems in reimplant TKA with hybrid technique
- Canal beads
  - an original concept → yes it started here

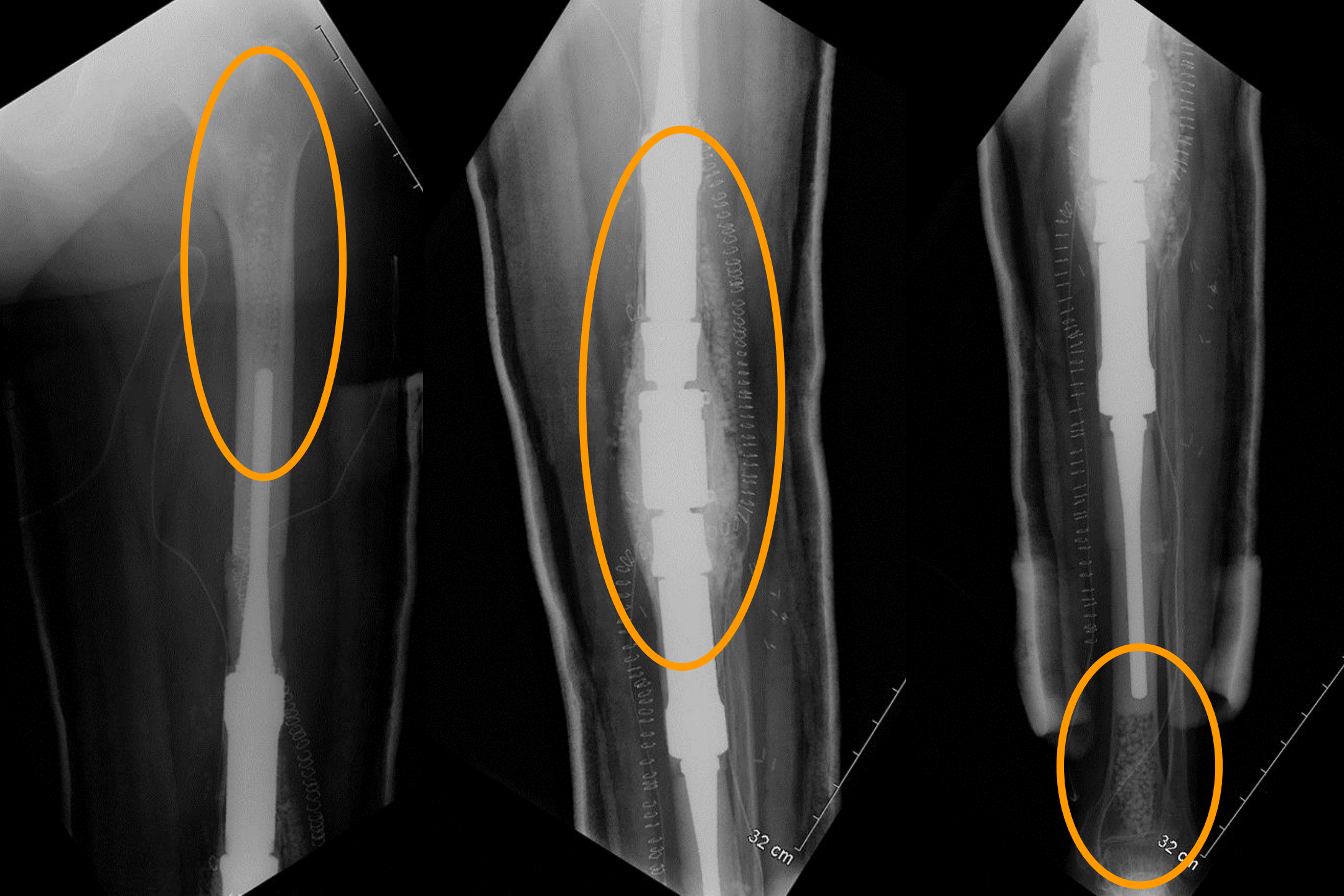


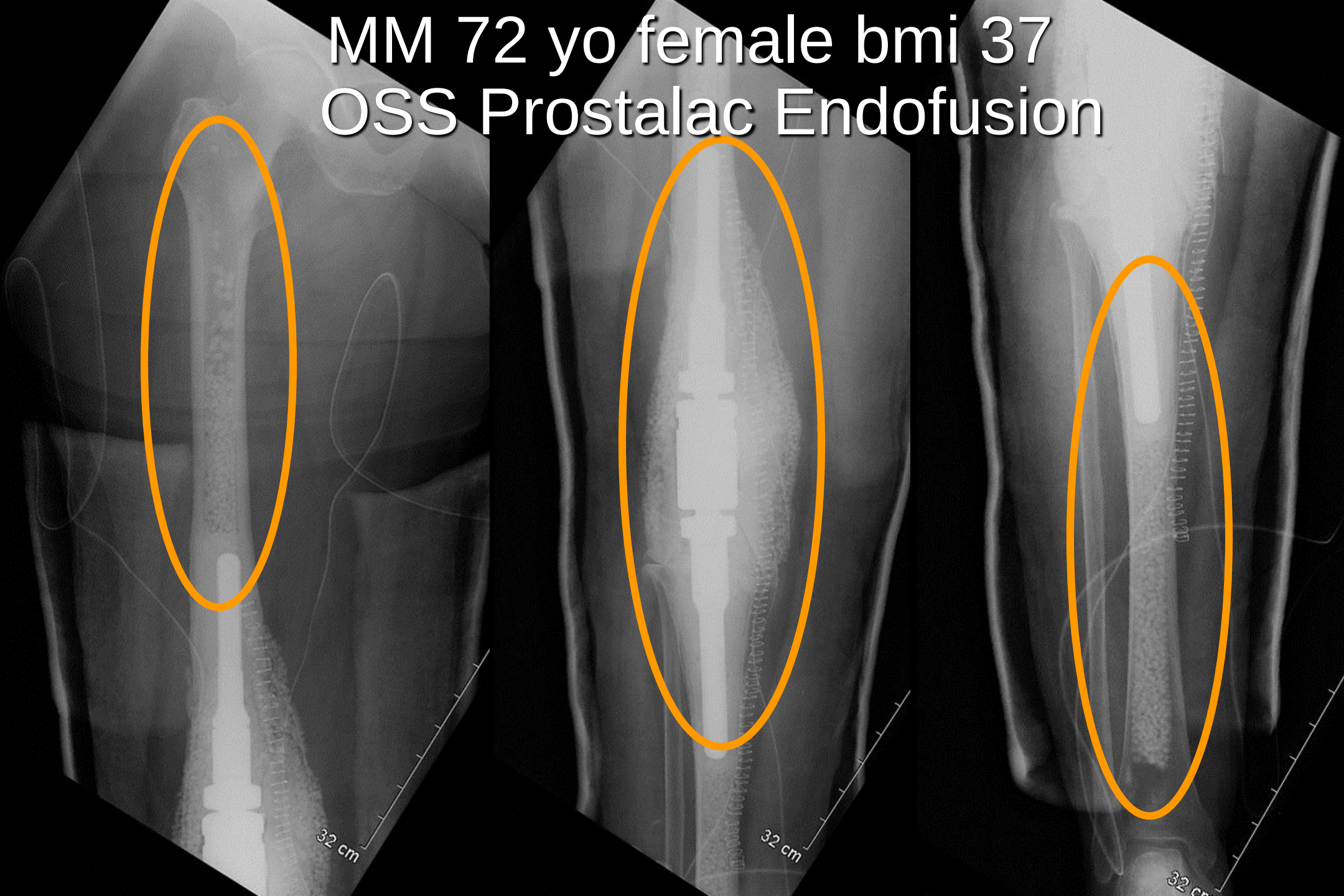



32 cm

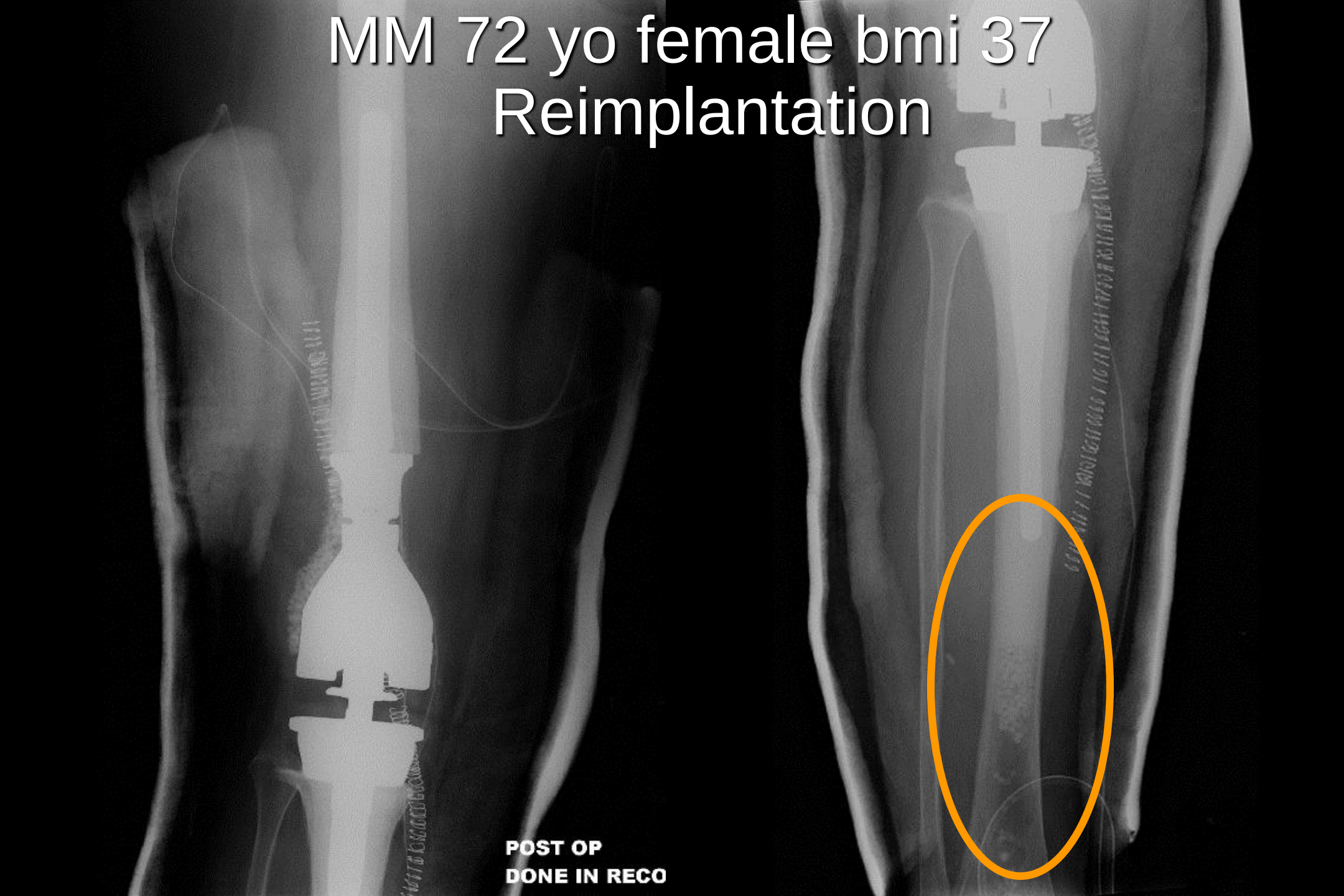



HN 67 yo male
bmi 32


32 cm


MM 72 yo female bmi 37
OSS Prostalac Endofusion
32 cm
32 cm

MM 72 yo female bmi 37
Reimplantation

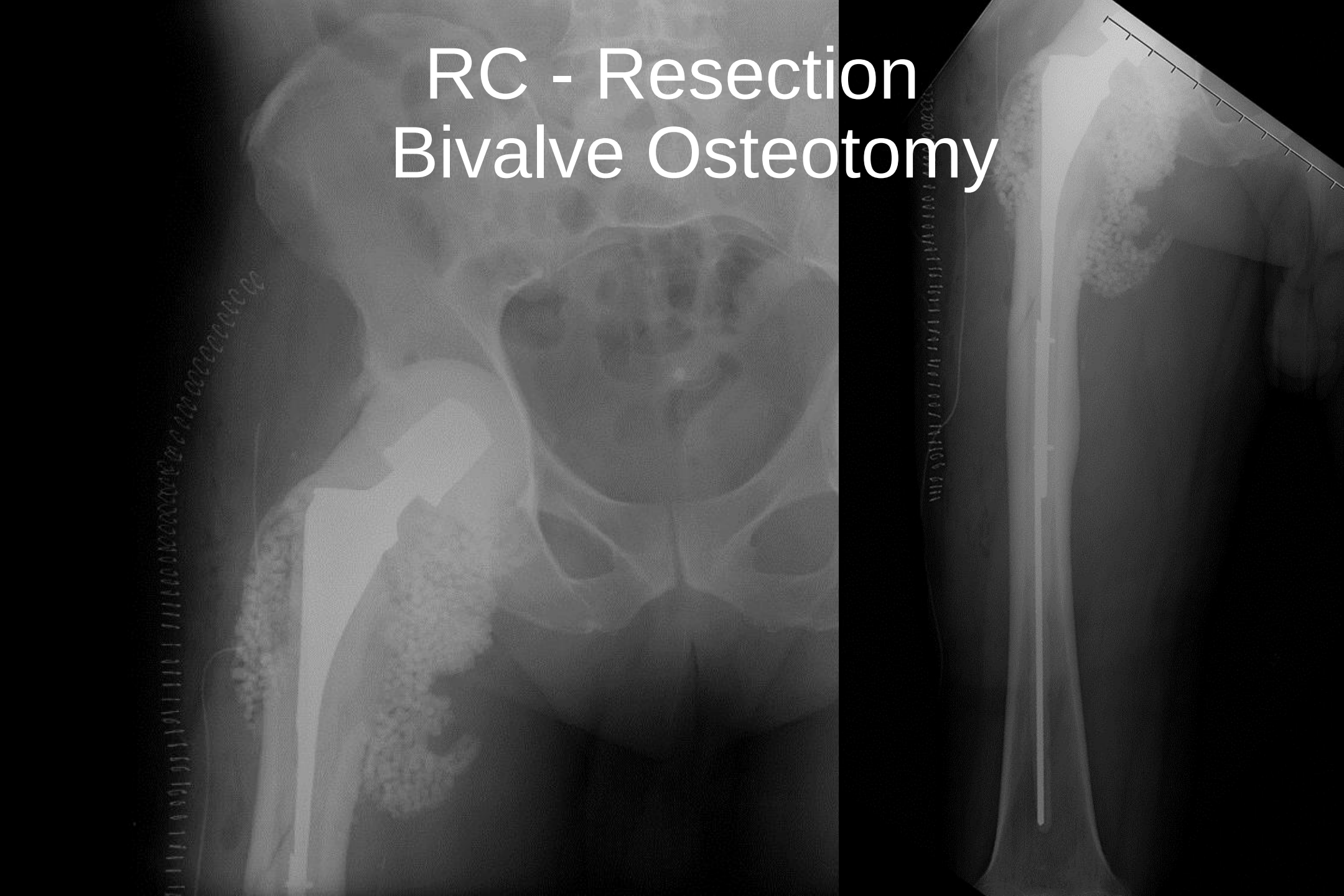


Case Study

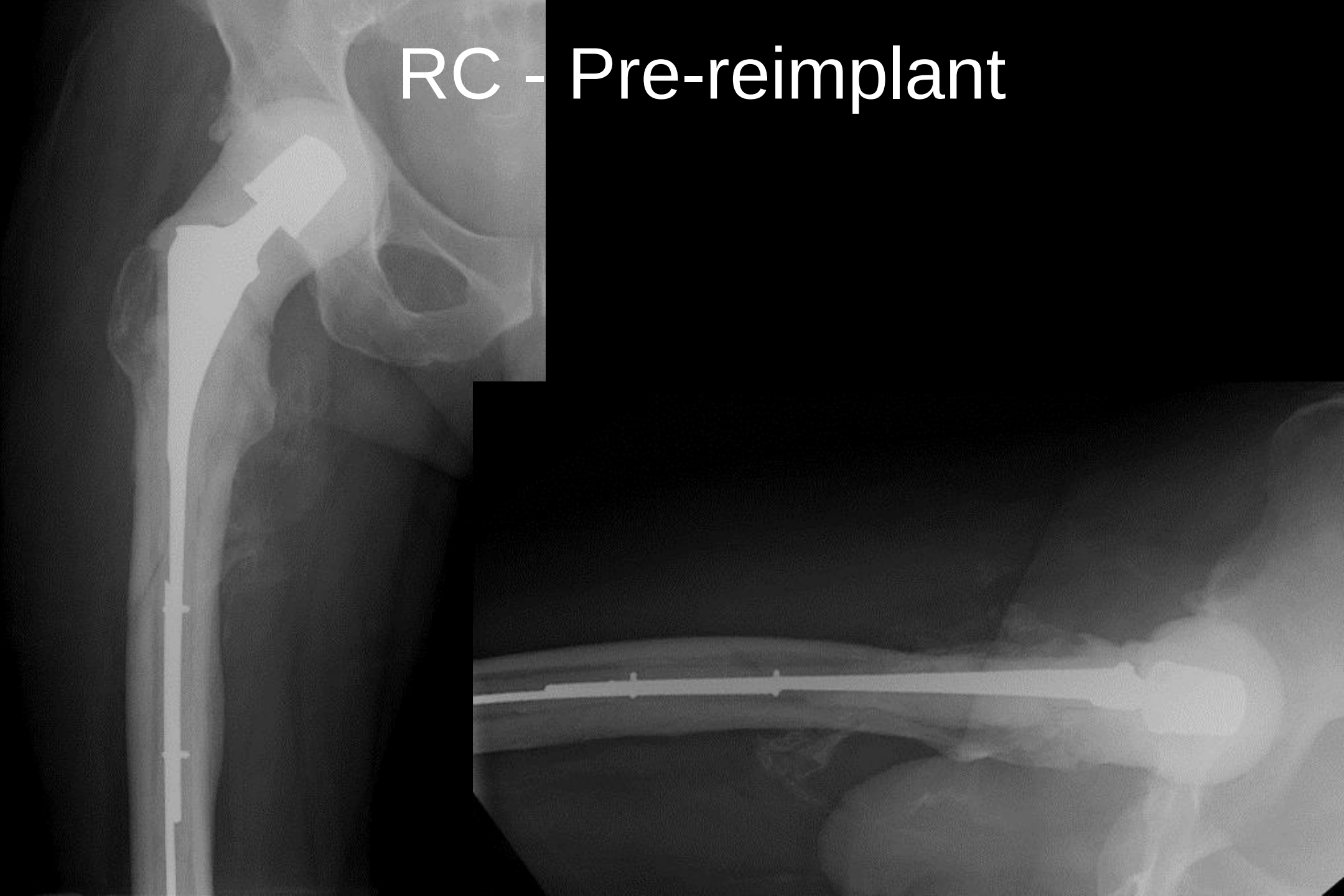
RC

- 63 yo ♂ - accountant
- Osteoarthritis
- THA → dislocation
- Revision x 2 → infection
  - mrsa

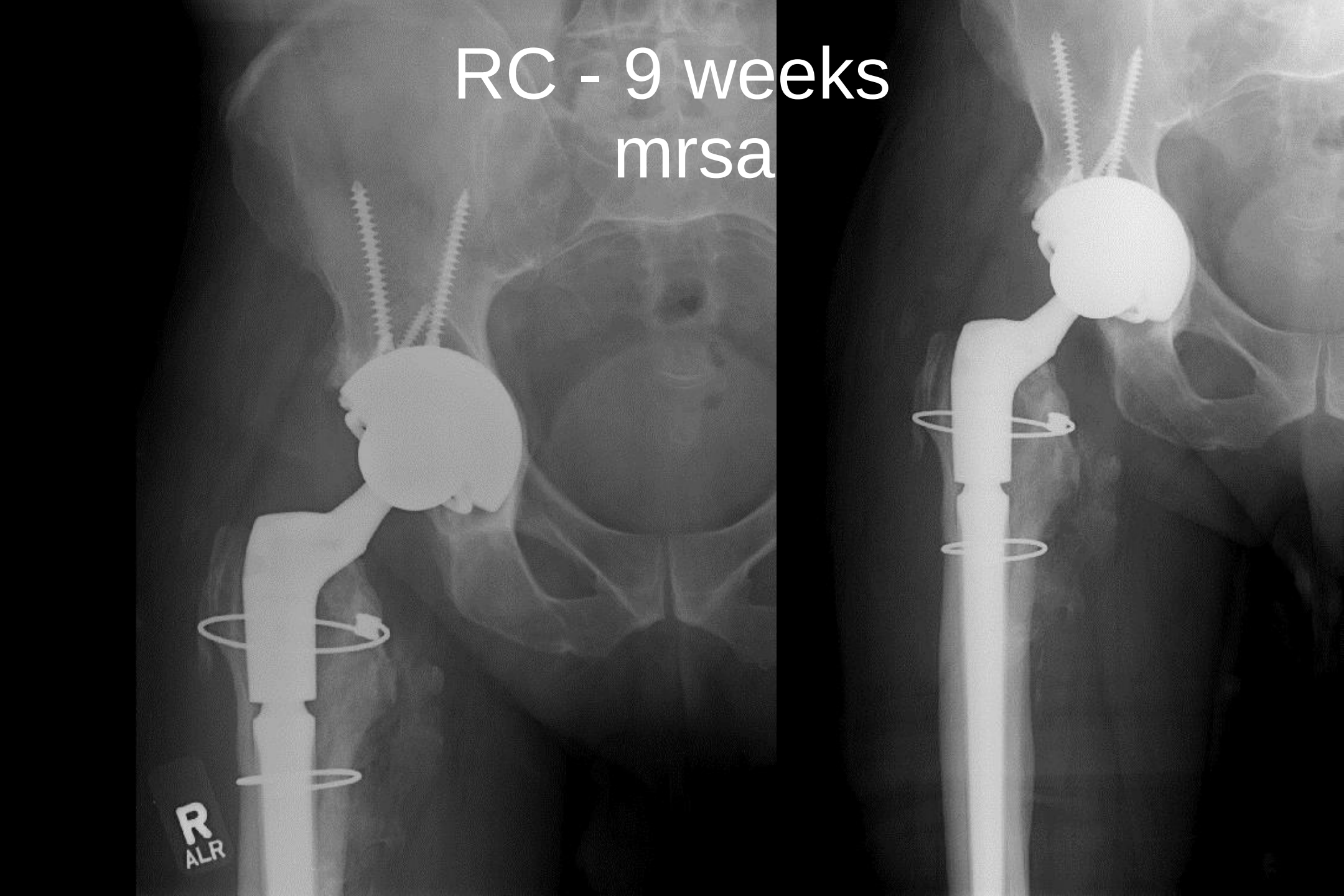
RC - Resection Bivalve Osteotomy



RC - Pre-reimplant

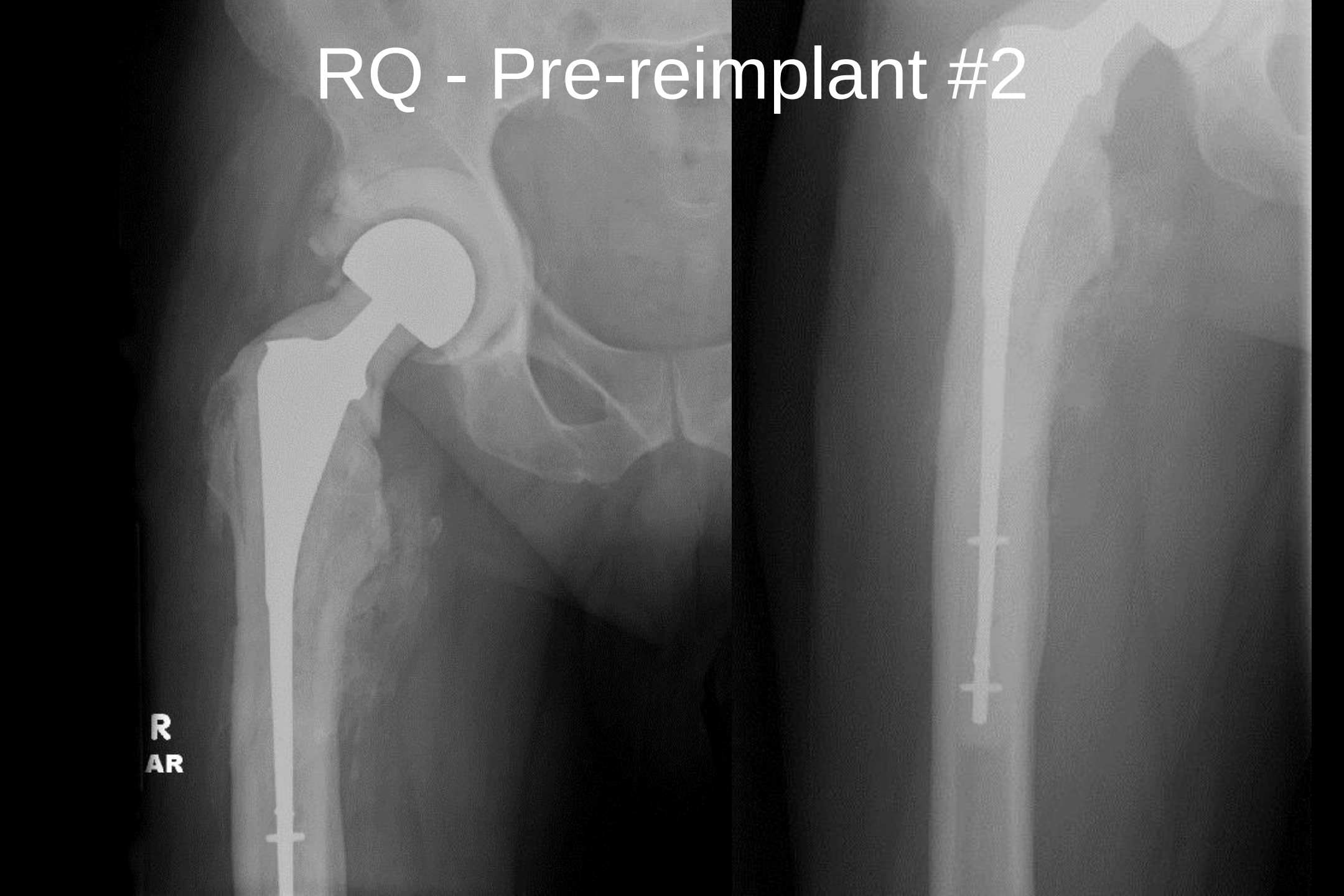



RC - Reimplant
Culture Negative
Stimulan
40cc

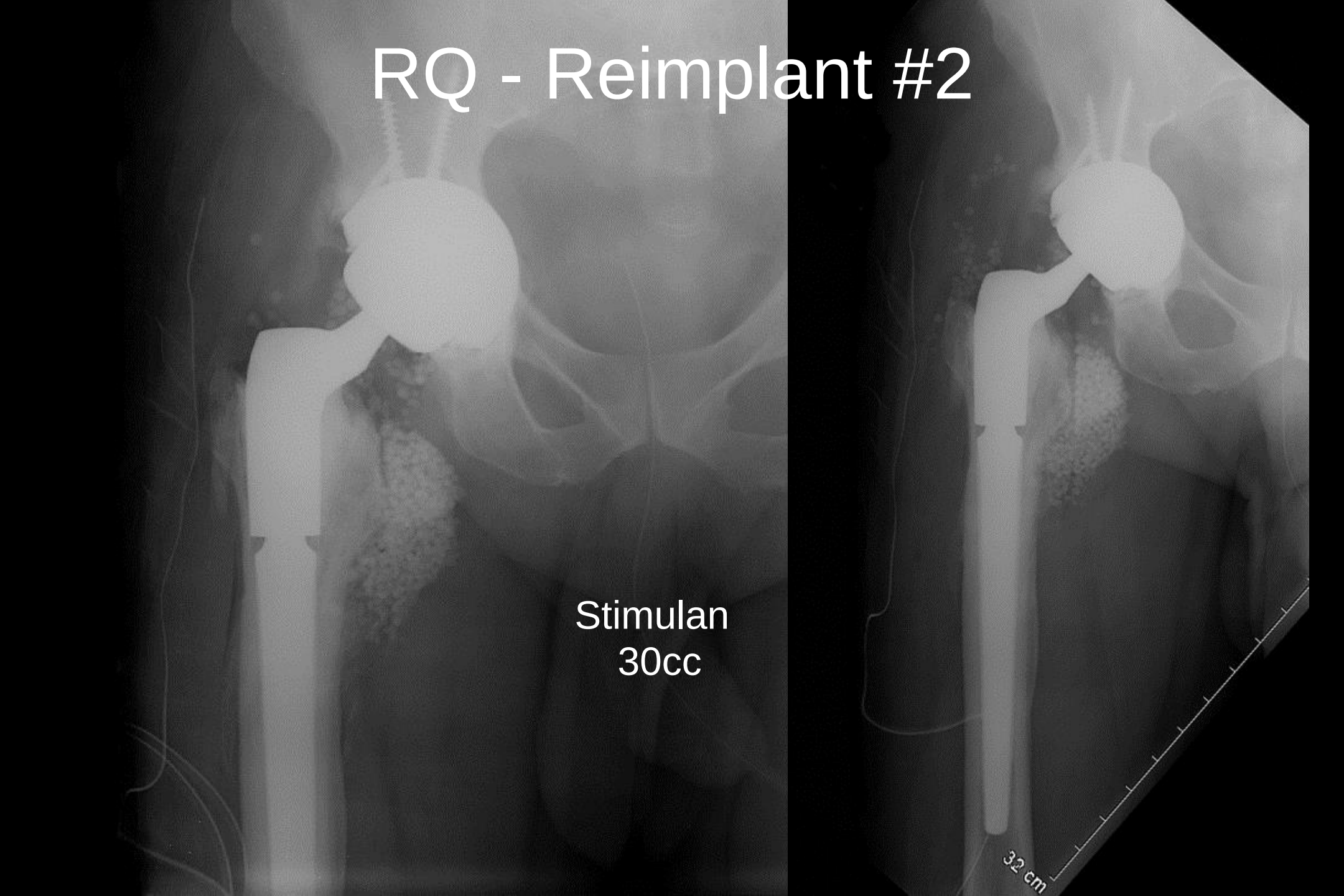

RC - 9 weeks
mrsa
R
ALR

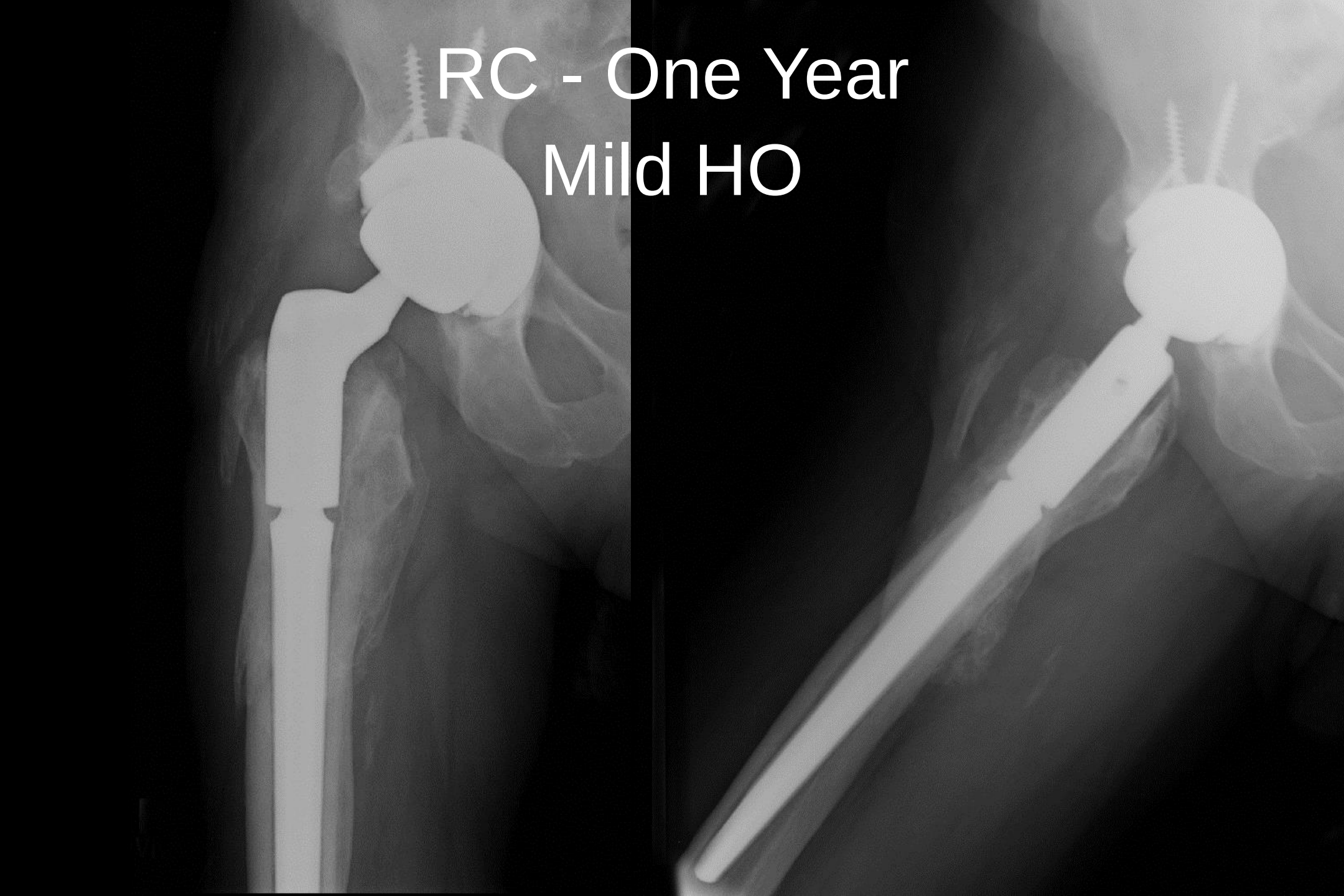

RC - Resection #2
mrsa

RQ - Pre-reimplant #2



RQ - Reimplant #2




RC - One Year
Mild HO

Case Study

RC - Lessons

- Inadequate debridement
  - somewhere in the system I left some biofilm & infection recurred
  - this case is landmark. it gave rise to the technique of using canal beads

Summary

Prosthetic Joint Infection

- Management is difficult, but often rewarding
- Risk reduction is ultimate goal
  - recognize your host
    - *c host → a game*
  - be aware of environment

Summary

Prosthetic Joint Infection

- Understanding biofilm is key
  - biofilm state = chronic infection
  - game over

Summary

Prosthetic Joint Infection

- Focus on the host, not the bug
- Staging the infection will help determine management
  - potentially will establish specific algorithms

Summary

Prosthetic Joint Infection

- High dose antibiotic cement functional spacer is a very effective treatment tool
  - high priority

Summary

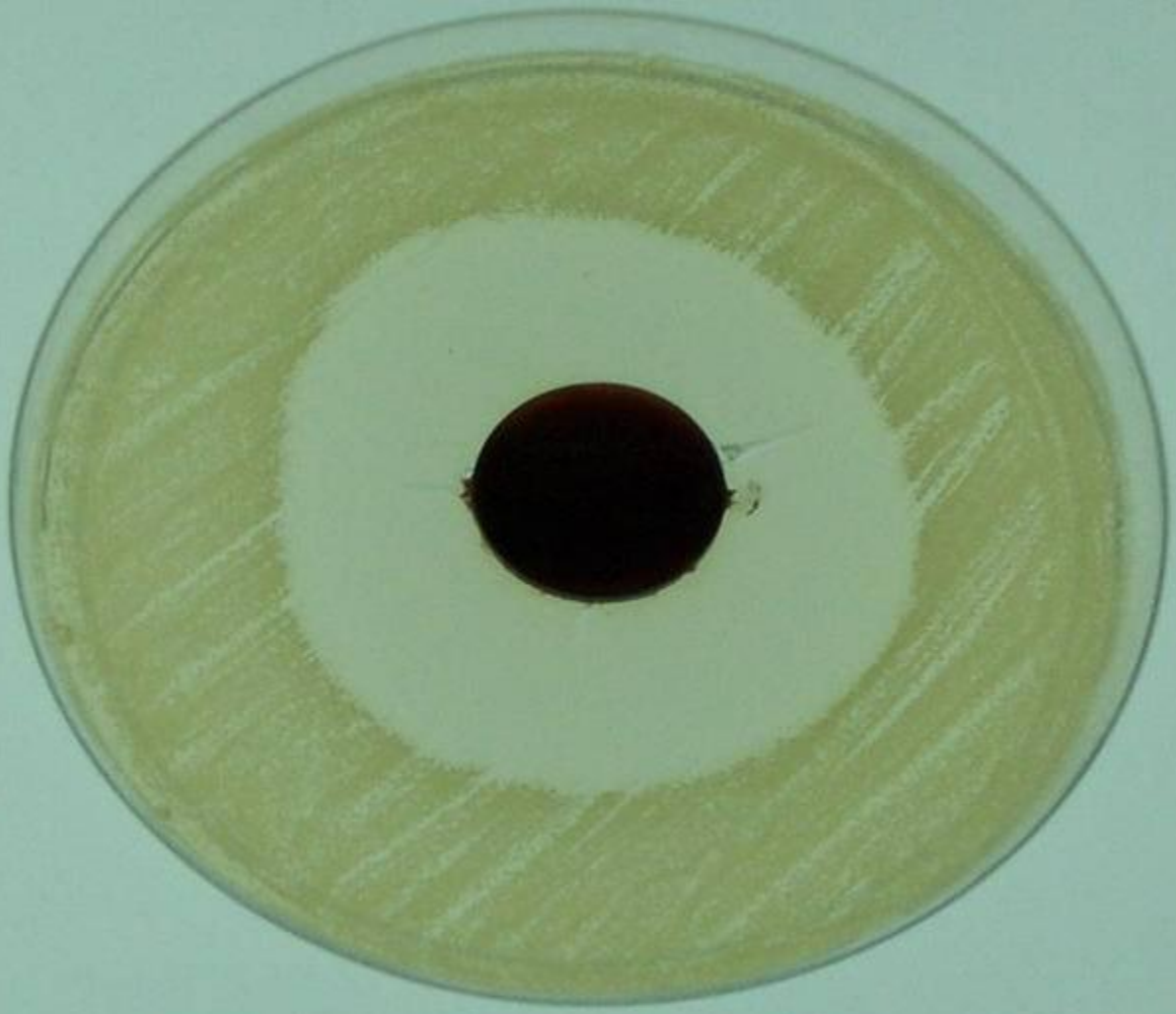
Prosthetic Joint Infection

- Muscle flaps are your friend
  - dead space management where cement spacer can’t help
  - knee wound coverage for compromised wound

Future Treatment PJI

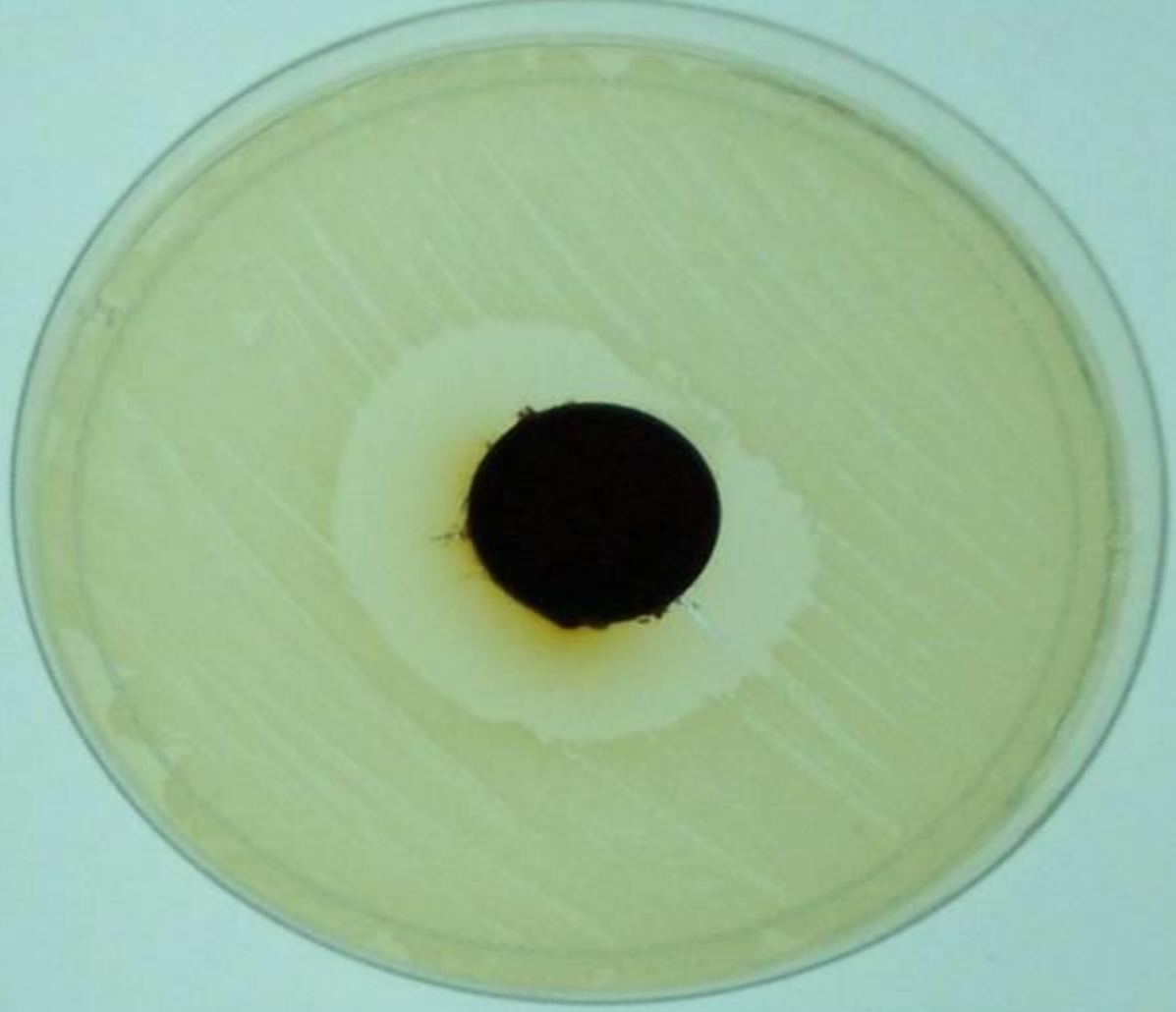
Near Term

- Codify staging system for multicenter trials
- Antibiotic coated cementless implants - maybe????



Staphylococcus aureus

Post ETO Titanium Disk
50/50 Minocycline/Rifampin Coated



Escherichia coli

Post ETO Titanium Disk
50/50 Minocycline/Rifampin Coated

Future Treatment PJI

Near Term

- Biofilm test kit - IP ejm
  - in vivo test
  - common structure to all biofilms
  - amplification assay
  - immediate result

Future Treatment PJI

Intermediate Term

- Biofilm dispersant molecules
  - highest priority!
  - potentially most cost effective treatment since the introduction of Charnley LFA

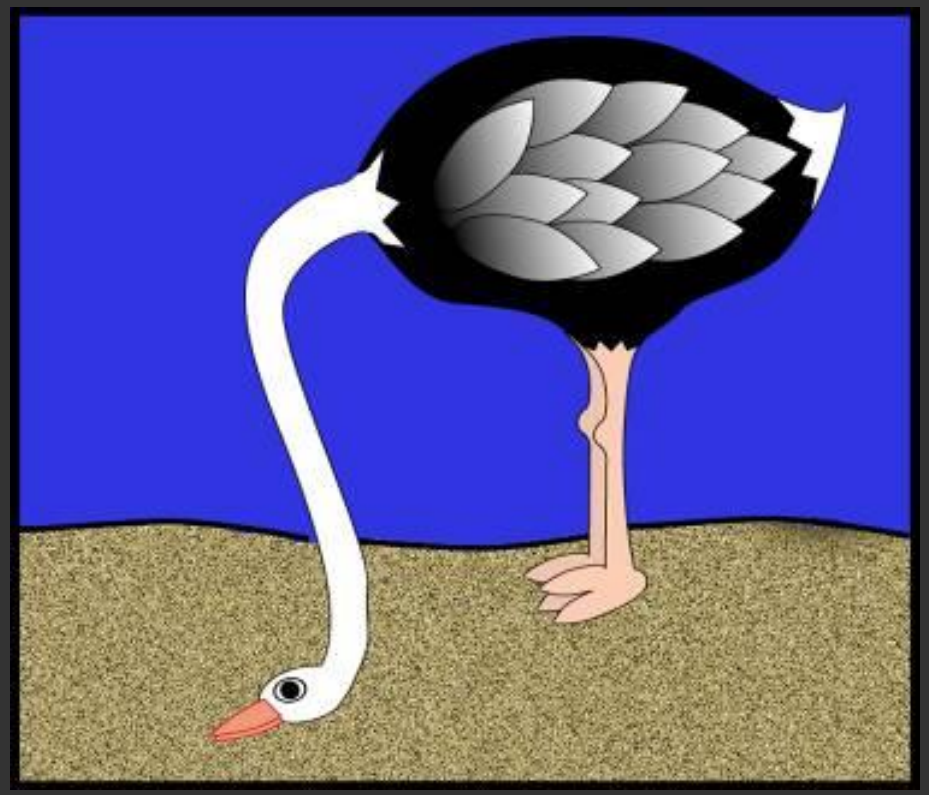
Future Treatment PJI

Long Term

- Biofilm modifying agents
  - quorum blocker molecules
  - biofilm dissolution molecules
- Biologic coatings on implants
- Host modifying agents
  - immune boosters

Lastly

Wound Drainage
Don’t Procrastinate !!



Bacteria Management Floor

Wound Drainage ≥ 5 days

- THA
  - 42% increase infection risk/day
- TKA
  - 29% increase infection risk/day

VP Patel JBJS 89A 1:33 07’

Prosthetic Survival

"Regulation of the surgeon and not the prosthesis is the means of achieving a successful result"

Prof. John Older MD

40th Year Celebration of John Charnley
San Carlos de Bariloche Argentina
03 Sept 2007

Summary

Surgeon Ownership

- Accept the responsibility of providing the patient the best chance for an aseptic reconstruction
- In reality, no one else really cares
  - aorn → push back

Trench Presence Does Matter!

California Orthopaedic Association

Prosthetic Joint Infection

Thank You

Indian Wells, USA
26 April 2015

L.A. Orthopedic Institute